Nurse-Led Behaviour Change Interventions to Improve Medication Adherence in Patients with Cardiovascular Disease

By

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Declaration of Original Authorship

I, **Ali Hussein Alek Al-Ganmi** declare that this thesis, is submitted in fulfilment of the requirements for the award of Doctor of Philosophy-Adult Nursing, in the Faculty of Health at the University of Technology Sydney. This thesis is wholly my own work unless otherwise reference or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis. This document has not been submitted for qualifications at any other academic institution. This research is supported by the Australian Government Research Training Program.

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Dedication

بسم الله الرحمن الرحيم

In the name of Allah the merciful, and prayer and peace upon the best of his creatures.

I dedicate this dissertation to my family that have granted me the continuous support throughout the entire PhD journey. I dedicate this dissertation to the cardiac patients that have granted me the privilege of sharing their experiences with taking cardiac medications and their stories about their life over the past two years. They have become my teachers-each one of them a true hero – surely, we have walked together on sacred ground.

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Overview of the Thesis

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Chapter Two: This chapter presents a systematic review of randomised controlled trial studies describing the best available evidence on the effectiveness of interventions suitable for delivery by nurses, designed to enhance cardiac patients' adherence to their prescribed medications. This chapter is based on a published paper: (Al-Ganmi et al. 2016).

Chapter Three: This chapter presents survey results determine and compare the level of adherence to cardiac medications and factors predictive of medication adherence in patients with cardiovascular disease admitted to a cardiac ward or attending cardiac rehabilitation in Australia. This chapter is based on a revised version of the second paper was submitted to the Journal of Nursing and Health Sciences: Al-Ganmi A., Perry L., Gholizadeh L., & Alotaibi A., (2019) Medication adherence and predictive factors in patients with cardiovascular disease in Australia. Revised version submitted to Journal of Nursing and Health Sciences.

Chapter Four: This chapter presents the findings of the multi-centre comparison study evaluated and compared adherence to cardiac medications and potentially predictive factors based on the Theory of Planned Behaviour (TPB) in patients with cardiovascular disease admitted to hospital and attending cardiac services in Australia and Iraq. This chapter is based on a paper published in Collegian: (Al-Ganmi et al. 2019).

Chapter Five: This chapter presents the proposed protocol, designed to pilot an RCT as a suitable test of the effectiveness of an evidence-based, nurse-led intervention in promoting of medication adherence. This chapter is based on a published paper: (Al-Ganmi et al. 2018).

Chapter Six: This chapter presents the overall discussion of the main findings of the two surveys of this study and wraps up the findings of this thesis in relation to its strengths and limitations.

Chapter Seven: This chapter presents the conclusions of this study and sets out the implications of this work and makes recommendations for, clinical practice, education, policy, and future research.

List of Abbreviations

ABS	Australian Bureau of Statistics
ACE	Angiotensin-Converting-Enzyme (ACE) Inhibitors
ACS	Acute Coronary Syndrome
AHA	American Heart Association
AIHW	Australian Institute of Health and Welfare
ARMS	Ability to Refill Medication Scale
BaMQ	Belief about Medication Questionnaire
CAD	Coronary Artery Disease
CR	Cardiac Rehabilitation
CCB	Calcium Channel Blockers
CHD	Coronary Heart Disease
CNC	Clinical Nurse Consultant
CVD	Cardiovascular Disease
ED	Emergency Department
IHD	Ischaemic Heart Disease
MAQ	Medication Adherence Questionnaire
MASES-R	Medication Adherence Self-Efficacy Scale-Revised
MI	Myocardial Infraction
MINT	Motivational Interviewing
MOH	Ministry of Health
NHMRC	Australian National Health & Medical Research
MSSS	Medications Social Support Scale
PBS	Australian Pharmaceutical Benefit Scheme
POWH	Prince of Wales Hospital
PDC	Proportion of Day Covered
RCT	Randomised Controlled Trial
TM	Text Message
UK	United Kingdom
USA	United States of America
WHO	World Health Organisation

Keywords

1. Medication Adherence
2. Medication non-Adherence
3. Cardiovascular Disease
4. Predictive Factors
5. Australia
6. Iraq
7. Cardiology
8. Cardiac Nursing
9. Medication Refill
10. Medication Self-Administration
11. Beliefs about Medication
12. Culture
13. Theory of Planned Behaviour
14. Cardiac Rehabilitation
15. Rehabilitation Nursing
16. Self-Efficacy
17. Social Support
18. Cardio-protective
19. Education
20. Motivational Interviewing
21. Nurse-Led Intervention
22. Nursing
23. Text Message
24. Randomised Control Trial
25. Pilot

Conference Papers and Publications Arising from the Thesis

Al-Ganmi A.H., Perry, L., Gholizadeh, L. & Alotaibi A.M. (2016). Cardiovascular medication adherence among patients with cardiac disease: a systematic review. ***Journal of advanced Nursing***, 72, 3001–3014. .

Al-Ganmi A.H., Perry, L., Gholizadeh, L. & Alotaibi A.M. (2016). Cardiovascular medication adherence among patients with cardiac disease: a systematic review. Cardiovascular Rehabilitation Association CRA NSW/ACT Inc (Stages in the Patient's Journey) 2016 Annual Scientific Meeting at Charles Perkins Centre at University of Sydney, October 24th 2016.

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Definition of Terms for this thesis

Adherence

The extent to which the patient’s behaviour matches agreed recommendations by the prescriber (Horne et al. 2005).

Adherence (Operational Definition)

The extent to which a patient takes prescribed medications according to the dosage and frequency recommended by the provider (Vrijens et al. 2012).

Medication Adherence

The extent to which a person’s behaviour (taking medications, following a recommended diet and/or executing lifestyle changes) corresponds with the agreed recommendations of a healthcare provider’ (Sabaté 2003).

Health Behaviour:

An action taken by a person to maintain, attain, or regain good health and to prevent illness. Health behaviour reflects a person’s health beliefs (Mosby’s Medical Dictionary 2009).

Behaviour Change

A broad range of activities and approaches which focus on the individual, community, and environmental influences on behaviour (Stedman's Medical Dictionary for the Health Professions and Nursing - Australia/New Zealand Edition 2005).

Cardiac Disease

A structural or functional abnormality of the heart, or of the blood vessels supplying the heart, that impairs its normal functioning (The American Heritage Medical Dictionary 2007).

Cardiovascular Disease (CVD)

Any disease that affects the cardiovascular system, principally cardiac disease, vascular disease of the brain and kidney, and peripheral arterial disease (Fuster & Kelly 2010).

Coronary artery disease (CAD), Coronary Heart Disease (CHD), or Ischaemic Heart Disease (IHD)

Narrowing of the lumen of one or more of the coronary arteries, usually due to atherosclerosis; leading to angina pectoris, myocardial infarction or congestive heart failure (Stedman 2005).

Acute Coronary Syndrome (ACS)

A classification encompassing clinical presentations ranging from unstable angina through myocardial infarctions not characterised by alteration in Q waves. The classification sometimes also includes myocardial infarctions characterised by altered Q waves (Mosby's Medical Dictionary 2009).

Self-Efficacy

A person's estimate or personal judgment of his or her own ability to succeed in reaching a specific goal, for example continuing at a prescribed weight level (Farlex Partner Medical Dictionary 2012).

Abstract

Introduction: Cardiovascular disease (CVD) is the leading cause of mortality worldwide, with medication non-adherence a suboptimal, poorly prioritised and challenging health problem in both developed and developing nations. Treatment of CVD for most patients comprises lifelong lifestyle changes and regular medication. Adherence to recommended treatment can be promoted by nurse-led interventions.

Aim: The overarching aims of this thesis were to develop a widely-applicable, evidence-based nurse-led intervention tailored to address factors predictive of poor adherence to medication regimes in patients with CVD who had been admitted to an acute hospital as an acute cardiac care or those who attend cardiac rehabilitation, and to design a protocol to trial this intervention. Objectives were:

Paper 1: To critically appraise and synthesise the best available evidence on the effectiveness of interventions suitable for delivery by nurses, designed to enhance cardiac patients' adherence to their prescribed medications.

Paper 2: To identify factors predictive of medication adherence in patients with cardiovascular disease admitted or attending hospital in Australia.

Paper 3: To compare factors associated with medication non-adherence in patients with CVD in developed and developing nations (Australia and Iraq).

Paper 4: To design a protocol suitable to test the effectiveness of an evidence-based nurse-led intervention in promotion of medication adherence in patients with CVD who admit to in-patient for acute cardiac care or those who attend cardiac rehabilitation.

Methods: Using established methods, a systematic review was conducted to identify effective nurse-led medication adherence interventions for patients with CVD. Cross-sectional surveys were conducted with 120 and 126 patients with CVD who were inpatients of a cardiac ward or attending cardiac out-patient care in acute tertiary hospitals in Sydney, Australia and Baghdad, Iraq, respectively. Medication adherence was assessed using the Medication Adherence Questionnaire; factors potentially predictive of medication non-adherence were assessed using validated instruments and modelled using regression analysis. A pilot randomised controlled trial was proposed to test the hypothesis that a theory-based, nurse-led, multi-faceted intervention comprising motivational interviewing techniques and text message reminders can enhance medication adherence in cardiac patients compared to standard care alone.

Results: Systematic review findings suggested that nurse-led interventions applying motivational interviewing and text messaging offer most promise. In the Australian study, participants from cardiac rehabilitation reported significantly lower adherence than ward in-patients. The comparative study showed significantly poorer adherence to cardiac medications in Iraqi than Australian patients. The ability to correctly self-administer and refill medications, and beliefs about medications, independently predicted cardiac medication adherence behaviour in both countries.

Conclusion: Nurse-led interventions that incorporate elements of motivational interviewing plus text messaging have the potential to improve medication adherence of patients with CVD through targeting patients' ability to self-administer and refill medications and their beliefs about these medications.

CHAPTER 1 Introduction

1.1 Introduction

In recent decades the rapid rise of coronary heart disease (CHD) has become a global health concern (Zhu et al. 2015) which challenges both patients and healthcare providers. These challenges include the emergence of new and increasingly complex medication regimes for cardiovascular disease (CVD) (Hauptman 2008). Medications have been shown to reduce the risk of complications of cardiac disease, post-discharge cardiac events, rehospitalisation and premature death. Adherence to medication is vital in realising optimal cardiovascular risk reduction for an individual at risk of CVD (National Heart Foundation of Australia 2011). For example, clinical trials have demonstrated that hypertension medications such as ACE inhibitors, angiotensin II receptor antagonists, β-blockade and calcium channel blocking agents can reduce the risk of myocardial infarction by 15% (Collins & MacMahon 1994), while non-adherence is associated with a 10–40% greater risk of hospitalisation and a 50–85% greater risk of mortality (Ho et al. 2008). Hence, significant non-adherence to medication regimes reduces the beneficial effects of these drugs, demonstrated in research studies. Non-adherence to medications is considered a hidden risk factor for patients with chronic disease including cardiac disease (Munger et al. 2007).

Medication non-adherence is a complex problem that poses an enormous health and economic burden. It is very common: it is estimated that up to 50% of patients with chronic disease do not follow their mediation regimes (Lee et al. 2006, Wilke et al. 2011), and has been reported as tending to occur more commonly among older populations and among patients who need multiple medications for chronic conditions (Menditto et al. 2015). Non-adherence is a multifactorial phenomenon, affected by factors including socio-economic status, health systems, disease states, pharmacological therapies and patient beliefs (Sabaté 2003). Supporting long-term adherence to medications is, therefore, an essential component of patient management, and requires effective interventions to help achieve sustained medication-taking.

1.2 The Healthcare System in Iraq

Iraq is an ancient country located in the Middle East, a region between Asia, Europe, and Africa, connecting the eastern and western parts of the world. Its population is estimated to be 32.2 million with annual growth of 2.3%, down from 3.1% in 1990 (Al Hilfi et al. 2013). It is divided into 18 provinces and Baghdad, the capital, ranks as one of the major population centres of the world with a population of six million. It is a middle-income country with a gross domestic product of US$223.5 billion. However, two decades of conflict (both international and intra-state), sanctions, and poor planning have reversed many of the gains made in the earlier decades of the twentieth century (Aziz 2003).

The Iraqi Ministry of Health (MOH) is responsible for planning, monitoring, and supervising health-related activities for the public and private sectors (Alwan 2004). Healthcare and public health services are provided through a nation-wide network that consists of a referral system, starting at primary care centres in the community, through secondary-level hospitals in provincial capitals, to tertiary hospitals in the major cities (The Iraqi Ministry of Health 2012). The public sector provides primary, secondary, and tertiary health services (Al Hilfi et al. 2013). The emphasis of the government on primary healthcare over the last two decades has made the public sector the main provider of primary healthcare services across the country, some provided free of charge. The public sector provides a considerable part of the secondary and tertiary health services in the provinces while the private sector, also a significant provider of healthcare, focuses on secondary and tertiary healthcare in urban areas. There are many non-governmental organisations active in the health sector (Al Hilfi et al. 2013).

Iraq has a total of 229 public hospitals, including 61 teaching hospitals. Additionally, there are 92 private hospitals, mainly located in the major population centres (Al Hilfi et al. 2013). Iraq is in the process of rebuilding following the recent devastating war and subsequent insurgency. Despite ongoing security issues, investment in the healthcare market has stabilised over the past few years (Alwan 2013).

There remain deficiencies in the healthcare system, and Iraq suffers from a shortage of medical services such as out-patient cardiac rehabilitation centres (Business Monitor International 2015). The barriers to providing local people with optimum healthcare are predominantly due to a lack of resources, including out-patient cardiac rehabilitation centres, qualified nurses, and available spaces in which to establish these centres. In particular, the shortage of human resources limits the number of facilities that can be upgraded. Staffing underserved areas with qualified healthcare providers may require incentives to make these desirable career options. In addition, public hospitals do not have the flexibility to manage their services individually, because budgets and procurement procedures are handled centrally. Problematic connections between the finance and planning directorates of the MOH are thought to be responsible for many of these difficulties (Aziz 2003). Further, there has been delay by the MOH in developing appropriate policy (Al Hilfi et al. 2013). Governance remains heavily centralised and is not transparent (Business Monitor International 2015).

In Iraq, there is no private health insurance, or co-payments or fees for pharmaceuticals. The whole population is covered by a public health services, public health insurance or social health insurance, and policies direct that people in Iraq receive public healthcare and medicines free of charge or for a nominal fee of US$0,43, with concessions for elderly patients to receive medicines free of charge (Hamza 2015). The MOH distributes pharmaceuticals to the public and private sectors after obtaining permission from the Drug National Quality Control Laboratories (DNQCL). The government has the responsibility to distribute pharmaceuticals without cost to the patients and users of public sector health services. KIMADIA (the state company for importation and distribution of drugs and medical appliances) is supported by the government budget. KIMADIA is responsible for procurement, storage and distribution of medicines for chronic conditions such as CVD (Alwan 2004). The government pays pharmaceutical companies through KIMADIA and public sector patients receive medications without cost as both inpatients and outpatients in most parts of Iraq (Hamza 2015). Patients with CVD are provided with a special chronic disease card which enables them to access their prescribed medications from public primary healthcare clinics and pharmacies with no significant cost. However, there is limited support available in the public service; supply of medications and medicine coverage is insufficient (World Health Organisation 2011) and due to shortages, unavailability and the interrupted supply of cardiovascular medications this system is not always effective. In the public health sector, the supply of medicine is insufficient to cover the full period of patients' treatment (Shabila et al. 2012). Medications for patients with CVD are not always available, which can negatively impact their health (Alwan 2013). This mean that in Iraq, most patients pay for prescribed medications; the cost is not covered by any insurance, and there is no system for reimbursement of money spent by the public on private prescriptions. This makes patients in Iraq sensitive to the value of medications and services (Sharrad et al. 2009) and ensures that the availability of medications at affordable prices is a public health priority.

Many of the country's most pressing needs are for public health interventions, yet these are not fully addressed as the government is still struggling to restore basic functions (Business Monitor International 2015), and Iraq is in need of public and private hospitals specialising in cardiac care as well as other healthcare services. The lack of official statistics on healthcare services, in addition to mismanagement and endemic corruption (Al Hilfi et al. 2013), make any evaluation of the healthcare system difficult (Garfield & McCarthy 2005). Due to the struggles of the Iraqi health system over the past decades, in- and out-patient health services including cardiac services need re-organising and restructuring as part of the overall health system. Direct and appropriate action to improve the primary care system is needed to foster a prevention-oriented system, targeting cardiac care services and providing momentum for behaviour change in areas such as medication adherence for patients with CVD. Iraq needs a strong public health agenda to develop policy initiatives for primary and secondary prevention programmes, and to improve access to services for vulnerable populations.

1.3 The Healthcare System in Australia

Australia's healthcare system includes a multifaceted variety of public and private providers, settings, participants and supporting mechanisms (Australian Institute of Health and Welfare 2016). Health services are provided by a variety of organisations and health professionals, including hospitals, clinics, pharmacies, government and non-government agencies: medical practitioners, nurses, allied and other health professionals. Together, they deliver a wide range of services, from public health and preventive services in the community to primary healthcare, emergency health services, hospital-based treatment in public and private hospitals, and rehabilitation and palliative care (Australian Institute of Health and Welfare 2016). Australia's federal, state and territory and local governments share responsibility for health, and they have many roles (funders, policy developers, regulators and service deliverers). Public hospitals are funded by the state, territory and Australian governments, and managed by state and territory governments. Private hospitals are owned and operated by the private sector but licensed and regulated by governments. The Australian Government and state and territory governments fund and deliver a range of other services, including population health programs, community health services, health and medical research, and Aboriginal and Torres Strait Islander health services. The Australian Government has responsibility for the universal public health insurance scheme (Medicare), for subsidising medical services and providing funding for primary health networks. Local governments, in addition to providing community-based health and home care services, have a significant role in public health and health promotion activities (Local Government NSW 2016).

Hospitals are an important part of Australia's health landscape, providing services to many Australians each year. A summary measure of their significance is the amount spent on them, estimated at $181 billion in 2016-2017; about 10% of Australia's gross domestic product and about Au$7,400 per person (Australian Institute of Health and Welfare 2018). Access to hospital services, the quality of the services, and their funding and management arrangements are under constant public scrutiny. In Australia, hospital services are provided by both public and private hospitals. State and territory governments mainly manage and are responsible for public hospitals. Public acute hospitals mainly provide 'acute care' for short periods, although some provide longer term care such as rehabilitation (Australian Institute of Health and Welfare 2014). In 2012–2013, there were 746 public hospitals and 592 private hospitals, with around 87,300 hospital beds in total.

Australian public hospitals are very diverse in size and the types of service provided for admitted and non-admitted patients, including emergency department services, outpatient clinics, emergency and planned (elective) care, maternity, and medical and surgical services. Australia's public hospitals employed about 275,000 full-time equivalent staff in 2012–2013, 45% of whom were nurses. Public and private hospitals are funded from a range of different sources, reflecting the types of patient they treat and the services they provide. Governments mainly fund emergency department and outpatient services, whereas admitted patient services are commonly funded by a combination of governmental and private (non-government) sources.

Both primary and secondary prevention of CVD are a national health priority. Around 88% of Australians are estimated to have visited a general practitioner at least once in 2005–2006, and the primary healthcare setting provides an early opportunity for addressing CVD risk. In Australia, many evidence-based guidelines are available to assist healthcare providers in assessing and managing CVD risk, but limited data are available on the management of overall CVD risk in general practice. For those at high risk who have not experienced a cardiovascular event, fewer than a quarter have been prescribed CVD preventive medications (Australian Institute of Health and Welfare 2014). It is recommended that secondary prevention guidelines endorse absolute-risk-based screening and the integration of risk assessment with multifactorial recommendations on CVD management, including medication adherence (Heart Foundation 2016). Such guidelines should be endorsed by the Australian National Health and Medical Research Council (NHMRC) and by all healthcare providers, including nurses. Availability of a single consolidated guideline could be an important initial step towards achieving substantial improvement in CVD risk management in general practice.

Studies report that adherence to cardio-protective medications is sub-optimal in both resource-limited and resource-rich countries (Chowdhury et al. 2013). This is a major problem internationally; as such, there may be lessons to learn from multi-national comparisons, studying the problem in different settings and contexts. Long-term cardiac medication adherence by Australian patients with CVD is unsatisfactory (McKenzie et al. 2015). To date, several investigations of medication adherence have been conducted with Australian patients with chronic conditions, but few adherence studies have been conducted with patients with CVD, and no published studies report adherence to cardiovascular medications in Iraq. Many medication adherence studies have been conducted in developed countries, but it is difficult to extrapolate the results of these studies to developing countries such as Iraq due to disparities in healthcare systems, social and cultural factors that affect health beliefs and practice (Sharrad et al. 2009). Medication non-adherence is a complex and multi-faceted problem, influenced by a wide range of sociodemographic and economic characteristics, behavioural and cognitive problems, medication complexity and social support systems (Marshall et al. 2012). Cultural differences among patients from diverse national backgrounds, racial and ethnic groups may contribute to disparities of cardiovascular medication adherence (Traylor et al. 2010). Cultural differences can influence patients' beliefs about medication and their perceptions of treatment, and differences in generations, household composition and religion may also create variability in beliefs and behaviours (Horne et al. 2004). Multiple different factors may, therefore, contribute to and drive medication non-adherence in developed and developing countries (Cooney et al. 2009), and comparison of these differences in relation to the different contexts may yield new insights.

1.4 Incidence and Prevalence of Cardiovascular Disease

The prevalence of CVD is increasing dramatically and it has emerged as a leading cause of death and disability worldwide, particularly in developing countries (Gaziano 2005). The American Heart Association (AHA) reported an estimated 83.6 million American adults (more than one in three) living with one or more types of CVD. Of these, 42.2 million are estimated to be 60 years and above (Go et al. 2014). CVD prevalence increases with age and affects one in six Australians, ranging from 35% of those aged 55–64 years to 62% of those aged 75 years and over (Australian Bureau of Statistics 2012). The number of Australian hospital separations due to CVD increased by 19% between 2001–2002 and 2011–2012 (Australian Institute of Health and Welfare 2014). The incidence of ischaemic heart disease (IHD) provides an estimate of sustained hypertension, which increases with age from less than 10% in the 25 to 34-year age group to almost 50% of people aged 75 years and over in developed countries (Nichols et al. 2014). Thus, the disease incidence has increased in many countries and the overall burden of CVD is high globally (Rashid et al. 2014). The prevalence and incidence of CVD has continued to increase in recent years. In Australia, as in other developed countries, this has occurred regardless of advances in medical technologies and prevention programs (Australian Bureau of Statistics 2012).

In low and middle-income countries (LMIC), the delivery of healthcare innovations and advanced treatment procedures is struggling to keep pace with the increased rate of adverse CVD risk factors associated with the socioeconomic transformations seen in these countries (Gaziano et al. 2010). Alarm has been raised by the World Health Organisation on the increasing burden of CVD and the disease severity and fatality rates seen in LMIC compared with high-income countries (Prabhakaran et al. 2018).

The largest increase in premature mortality attributable to CVD over the past 20 years has occurred in LMIC, with the number of deaths increasing from 7.21 million in 1990 to 12 million in 2013, a 66% increase (Roth et al. 2017). However, in high-income countries, mortality rates for CVD fell from 283 per 100,000 persons in 1990 to 160 per 100,000 in 2013, a 43% decline (Roth et al. 2017). The significant decline in mortality rates among high-income countries has been attributed to population-level changes in risk factors and, more recently, improvements in healthcare (Ford et al. 2007). Similarly, the growth and ageing of populations has increased the proportion of deaths attributable to CVD in many poorer countries and, as a result, the mortality gap between LMIC and high-income countries over the past two decades has narrowed (Roth et al. 2017). More recently, improvements in diet, tobacco control, and healthcare delivery appear to have contributed to better health outcomes (Kesteloot et al. 2006). The causes of the decrease in developed countries offer potential lessons for achieving similar results in developing countries. In addition, the contribution of improved treatment options (in the UK) was responsible for 40% of their reduction in CVD mortality, with a concurrent reduction in risk factors accounting for the majority of the decline (Davies et al. 2007).

Australia and Iraq are completely different countries for many reasons including family lifestyle, social life, culture and traditions as well as landscape. Both countries have seen increasing prevalence of CVD in recent decades, with healthcare systems attempting to reduce the burden of CVD by implementing national interventions. However, in Iraq the regulation of healthcare providers is limited (Al Hilfi et al. 2013), whereas in Australia, healthcare delivery is highly regulated.

1.5 Cardiovascular Risk Factors

One of the most important advances in cardiovascular research has been the identification of risk factors associated with CVD. Treatments have subsequently been developed and rigorously tested to modify these risk factors with the goal of preventing CVD. Risk factors are common across countries, with smoking, diabetes, hypertension, abdominal obesity, psychosocial factors, fruit/vegetable consumption, physical activity and alcohol consumption identified as potentially modifiable risk factors for CVD amongst patients from 52 countries (Yusuf et al. 2004).

Patients aged 45 years and above who have one or more risk factors are more vulnerable to CVD than younger people or those without risk factors. The prevalence of CVD increases with the presence of one or more major risk factors, such as: hypercholesterolemia, hypertension, diabetes, smoking, obesity, and physical inactivity (Australian Bureau of Statistics 2012), hence a large proportion of CVD risk is attributable to preventable factors, and risks are cumulative. A meta-analysis of 18 cohort studies revealed that the risk of cardiovascular events increased by 49.5% and 30.7% among men and women respectively by age 80 if they had two or more risk factors at the age of 45 years (Berry et al. 2012).

A few studies provide direct insights into the causes of recent increases in CVD incidence and mortality in LMIC. For example, in their study of the rise of CHD mortality in China from 1984 to 1990, Critchley et al. (2004) found that blood lipid increases were the largest contributor, responsible for 77% of increased CHD mortality. However, a significant body of research suggests that smoking tobacco (Bump et al. 2009) and rapid dietary changes associated with nutritional transition, along with decreasing levels of physical activity in many rapidly urbanising societies, play particularly important roles in the rise of CVD in developing countries (Stein et al. 2005). This has been seen in increasing obesity, changes in dietary patterns (Popkin et al. 2012), high prevalence of tobacco smoking (Maziak 2011) and large disparities in physical activity among populations in many Middle Eastern and North African countries (Rahim et al. 2014). However, the management of behavioural/lifestyle-related CVD risk factors at the individual and population level lies outside of the domain of healthcare systems in many LMIC (Wells et al. 2011).

1.6 Pathology of Cardiovascular Disease

Acute manifestation of CHD occurs when one or more of the coronary arteries become severely or totally blocked mainly by blood clots due to the disruption of unstable atherosclerotic plaque in the coronary artery, described as acute coronary syndrome (ACS) (Brunner et al. 2010). ACS consists of a constellation of ischaemia-induced syndromes such as myocardial infarction and angina pectoris (Topol & Califf 2002). Myocardial ischaemia occurs when coronary blood flow is occluded by a plaque and myocardial oxygen demands are markedly increased. Atherosclerotic plaques are derived from functional changes in the vascular milieu and sub-intimal collections of fat, smooth-muscle cells, fibroblasts, and intercellular matrix. This limits the ability to increase blood flow to meet increased myocardial demand, resulting in myocardial ischaemia at rest or with minimal stress. This usually occurs when the diameter of an epicardial artery is reduced by 50–80%: "patients experience clinical manifestations of myocardial ischaemia when thrombus composed of platelet aggregates and fibrin strands congest red blood cells reducing coronary blood flow" (Antman et al. 2013). Cell death subsequently occurs because the blockage deprives the heart muscle of oxygen-rich blood, leading to life threating arrhythmia such as ventricular tachycardia or ventricular fibrillation (Australian Institute of Health and Welfare 2010). The odds of survival decrease by 7% to 10% for each minute that the patient remains in ventricular fibrillation (Swanton & Banerjee 2008, Antman et al. 2013). However, CHD is not just an acute phenomenon but also a long-term chronic disease which affects patients' physical, psychological, behavioural and social function. The long-term determinants of functional status need to be understood in order to improve and maximise the functionality of patients with CVD (Sin et al. 2015).

1.7 Medication Non-Adherence as a CVD Risk Factor

In order to reduce the risk of recurrent cardiac events, patients need to reduce their CVD risk factors and adhere to their medication regimes, as medication non-adherence is a significant hidden cardiovascular risk factor, contributing to recurrent cardiac events, persistent symptoms and disease progression (Munger et al. 2007).

Improving the prescription of guideline-recommended medications has been associated with diminished mortality of 20% at one year after myocardial infarction; patient adherence to these medications has improved symptom management and decreased the risk of recurrent cardiovascular events (Baroletti & Dell'Orfano 2010). Repeated calls have been made for healthcare providers to assess patient adherence to medication, with appropriate intervention as necessary (National Council on Patient Information and Education 2007). A subjective self-report approach such as self-reported questionnaires is an effective method, as this is a relatively simple and inexpensive way (Al-Ganmi et al. 2016) to identify the level of adherence and adherence patterns for patients at risk of medication non-adherence. A simple and effective method is required to identify patients at higher risk for medication non-adherence in order to plan effective interventions to improve their medication adherence for chronic conditions. These methods should centre on applying evidence-based and rigorous interventions including behavioural interventions that can target patients' unhealthy behaviour patterns with long-term follow up to increase and sustain medication adherence and evaluate the impact of these interventions. Behavioural interventions to improve medication adherence have proven to be an effective strategy by targeting, shaping, or reinforcing specific behavioural patterns such as building skills and practicing medication taking activities, packaging and dosage modifications, and self-medication reminders (Al-Ganmi et al. 2016). Behavioural interventions also influencing medication adherence by appealing to patients' feelings, social relationships and social supports, by engaging in counselling, through supportive home visits, and family support. However, the evidence suggests that simple behavioural interventions such as text message reminders used by themselves are not sufficient to ensure adherence to cardiac medications (Adler et al. 2017).

1.8 Burden of Cardiovascular Disease

CVD imposes significant burden on individuals and healthcare systems. In 2004–2005 it accounted for 16% of the total burden of disease in Australia, which translated to AU$5.94 billion and equated to 11% of the country's total health expenditure (Australian Institute of Health and Welfare 2010). Mortality data showed CVD as the underlying cause of death for 34.3% (831 272) of all 2, 426, 264 deaths in 2006 in the US: more than cancer and accidents combined. This translates to 1 of every 2.9 deaths in this country (National Center for Health Statistics 2009, Lloyd-Jones et al. 2010). Mortality from CVD is predicted to reach 23.4 million in 2030 in the US (Cassar et al. 2009). Consistent with international trends, CVD is the single greatest cause of death in Australia, accounting for the deaths of 21,867 males and 23,755 females in 2011

(Australian Institute of Health and Welfare 2014). It was also the main reason of rehospitalisation, accounting for 524,000 hospitalisations in 2011–2012 (Australian Institute of Health and Welfare 2014). It has been estimated that men aged 55 years with at least two major risk factors are six times more likely to die from CVD by age 80, compared to men with none or one CVD risk factor (29.6% vs. 4.7% respectively) (National Heart Foundation of Australia 2011). In 2012, 43,900 deaths in Australia were attributed to CVD, indicating that one Australian dies from CVD every 12 minutes (Australian Bureau of Statistics 2014). Further, patients with CVD may suffer from disabilities such as physical symptoms, depressive symptoms and impaired functional status, which are closely related to poor health related quality of life (Heo et al. 2015). Patients' quality of life can be significantly compromised by CVD, contributing to severe physical, role, and social functioning impairment, and increasing psychological distress (Carels 2004). CVD is one of the leading causes of disability in Australia (Australian Institute of Health and Welfare 2008). According to an Australian survey on disability and ageing conducted in 1998, a rate of 126 per 100.000 people aged 45 years and over had one or more disabling conditions due to a heart attack (Heart Foundation 2005). Of these, 76.6% needed assistance or had difficulties with self-care, mobility or communication and 19.4% had no difficulties but used aids or equipment (Heart Foundation 2005). Patients with cardiac disease or comorbidity were reported to have greater healthcare utilisation, including more hospital admissions, longer stays in hospital and were more likely to have complications (Australian Institute of Health and Welfare 2008). Overall, mortality, hospitalisation and disabilities from cardiac disease vary by age, gender, and the presence of risk factors.

1.9 Cardiovascular Disease in Developed and Developing Countries

Cardiovascular disease (CVD) is the major cause of death in both developed and developing countries (Wirtz et al. 2016). In developed countries, the annual mortality associated with CVD in 2013 was 4 million people, with more than 1.4 million dying prematurely before the age of 75 years (Townsend et al. 2016). In Australia, CVD accounts for 18% of the total burden of disease (Janus et al. 2010) and was responsible for 43,963 deaths in 2016 and more than 490,000 hospital admissions in 2014–2015 (Heart Foundation 2016). According to the Australian Pharmaceutical Benefits Scheme (PBS), the total cost of CVD medications in 2015–2016 was AU$1.448 billion, comprising 20% of the total health expenditure (Australian Institute of Health and Welfare 2017).

Internationally, studies have shown that the rates of CVD are increasing, particularly in Middle Eastern countries such as Iraq where many people are at increased risk (Bovet et al. 2006). In Iraq, CVD accounted for 27,500 deaths in 2012, or 16.5% of total deaths from all causes (World Health Organization 2013), and the incidence of premature CVD is rising at an alarming rate (Mohammad et al. 2015). The Iraqi government subsidises the cost of a wide range of prescription medicines, including those for cardiovascular disease. The government's expenditure on health was $82.2 billion in 2008 with an estimated 39% spent on medications , about $247 per person (Al Hilfi et al. 2013).

In Iraq, there is no private health insurance and, the whole population is covered by a public health services, public health insurance or social health insurance, However, due to shortages and the interrupted supply of cardiovascular medications this system is not always effective and medications for patients with CVD are not always available. Standard post-discharge care includes cardiologist visits either in a public or private primary care facility (Ola et al. 2019). The prescribers in these settings optimise cardio-protective medications to achieve the target dose based on the patient's tolerance and haemodynamic profile. However, in reality the cost and availability of medications are potential obstacles to long-term persistence with therapy (Ola et al. 2019). As a consequence, the standard of treatment and care can be inadequate in Iraq and the healthcare system can be ineffective in managing long-term disease such as CVD (Alwan 2004).

1.10 Non-Adherence to Medication in Developed and Developing Countries

For many chronic conditions medications are necessary to prevent deterioration of patients' health status, and adherence to medications is required for them to be clinically effective (Conn et al. 2009). The rates of non-adherence in adult population have been shown to vary across multiple settings and countries, and in patients with a variety of chronic diseases; these discrepancies are as much due to methodological differences as true variation in rates. Where medications for long-term conditions are not taken as prescribed in developed and developing countries, rates of non-adherence ranging from 33%–88% have been reported. While these statistics are based on different methods of assessments and differing definition of adherence (Mills et al. 2006), they indicate consistently poor rates of adherence.

Unsatisfactory levels of medication non-adherence have been reported in developed countries of patients with chronic conditions who have difficulty maintaining adequate levels of adherence (Nieuwlaat et al. 2014) (**Table 1.1**). For example, one review demonstrated that medication non-adherence rates of patients with bipolar disorder were 41.5–43.0% in developed countries (Chakrabarti 2017), while Novick et al. (2010)) reported that the prevalence of non-adherence to antipsychotic treatment ranged from 20–56% in patients with schizophrenia in European Union countries. One study from Italy found adherence among Italian patients with chronic diseases was 39.3% among (Napolitano et al. 2016), while another found 59.9% of older adults had low levels of adherence (Menditto et al. 2015). In the United States, rates of medication non-adherence were found to be 67% in patients with hypertension (Muntner et al. 2011) and 65% in patients with heart failure (Hood et al. 2018); an overall non-adherence rate of 40.7% was found among patients with three comorbid diseases (CVD, diabetes mellitus and hypertension) (Marcum et al. 2013). A population-based cohort study conducted in Canada revealed that 74% of patients discharged following acute myocardial infarction were non-adherent one year post discharge, with high mortality rates (Jackevicius et al. 2008).

Non-adherence is even higher in developing countries (**Table 1.1**) mainly because of the lack of health resources and access to affordable medications (World Health Organisation 2003). Again, rates of adherence vary across settings, and within and between countries. Nonetheless, studies consistently report that adherence to chronic disease-related medications is sub-optimal (Chowdhury et al. 2013). In the developing nations of the Middle East, for example, non-adherence has been found to commonly range around 50–57% (AlHewiti 2014), including 54.8% in Saudi Arabia (Ahmed et al. 2017) but 75% in Palestine (Jamous et al. 2011); and 47% of Saudi Arabian patients do not adhere to hypertension medication regimes (Khalil & Elzubier 1997). The prevalence rate of medication non-adherence among patients from Iraq is not known since there is no published research from this area.

Poor adherence, whether to CVD medication regimes or any other, reduces the benefits achievable from medications and results in unnecessary hospitalisations and reduced quality of life (Hauptman 2008). Given how common it is in both developed and developing countries, more research is needed to understand the factors that predict non-adherence. Iraq, a major developing nation, has produced no studies in this area; Australia, a major developed nation, has produced only few (Al-Ganmi et al. 2019). There is clearly a need for further investigation across as well as within nations, to identify avenues that may prove valuable in developing interventions to improve adherence, in CVD and other chronic illnesses.

Table 1.1 Prevalence of non-adherence to medications in developed and developing countries

Author (Year)	Study type	Patients group	Location	Non-adherence rates
Developed Countries				
WHO (2003)	WHO Report	Chronic disease	Developed Countries	48–50%
Chakrabarti (2017)	Literature Review	Bipolar Disorder	Developed Countries	41.5–43%
Novick et al. (2010)	Prospective Study	Schizophrenia	European Union	20–65%
Napolitano et al. (2016)	Cross-sectional Study	Chronic Disease	Italy	39.3%
Menditto et al. (2015)	Cross-sectional Study	Older Adults	Italy	59.9%
Muntner et al. (2011)	Cross-sectional Study	Hypertension	USA	67%
Hood et al. (2018)	Retrospective Cohort Study	Heart Failure	USA	65%
Townsend et al. (2007)	Retrospective Cohort Study	HIV	USA	30%
Marcum et al. (2013)	Cross-sectional Study	CVD, Diabetes Mellitus, Hypertension	USA	40.7%
Morrison et al. (2015)	Cross-sectional Study	Hypertension	Netherland Hungary	24–70%
Tomaszewski et al. (2014)	Biochemical Screening	Hypertension	UK	25%
Jackevicius et al. (2008)	Population-based cohort Study	Acute Myocardial Infarction	Canada	74%
Byrne et al. (2015)	Cross-sectional Study	Diabetes Mellitus CVD	Ireland	57–69%
Ignacio et al. (2017)	Retrospective Cohort Study	CVD Chronic Inflammatory Disease	Spain	8–23%
González López-Valcárcel et al. (2017)	Retrospective Cohort Study	Acute Coronary Syndrome	Spain	84.2–90.7%
Australian Institute of Health and Welfare (2007)	Government Report	Patient with Statin Therapy	Australia	23%–60%
McKenzie et al. (2015)	Literature Review	CVD	Australia	14–43%
Reid et al. (2000)	Postal Questionnaire Survey	Asthma	Australia	57%
Simons et al. (2008)	Longitudinal Study	Hypertension	Australia	31–79%

Author (Year)	Study type	Patients group	Location	Non-adherence rates
Developing Countries				
Al Qasem et al. (2011)	Literature Review	Chronic Disease	Middle Eastern Countries	1.4–88%
AlHewiti (2014)	Cross-sectional Study	Chronic Disease	Middle Eastern Countries	50–57%
Rwegerera et al. 2018	Cross-sectional Study	Diabetes Mellitus	Botswana	41.8%
Jamous et al. (2011)	Cross-sectional Study	Diabetes Mellitus	Palestine	75%
Ahmed et al. (2017)	Cross-sectional web-based Study	Diabetes Mellitus	Saudi Arabia	54.8%
Khalil & Elzubier (1997)	Prospective Study	Hypertension	Saudi Arabia	47%
Kokturk et al. (2018)	Cross-sectional Study	COPD	Saudi Arabia	64.2%
Woimo et al. (2017)	Cross-sectional Study	Tuberculosis	Ethiopia	24.5%
Al-Noumani et al. (2017)	Cross-sectional Study	Hypertension	Oman	66%
Al Qasem et al. (2011)	Literature Review	Hypertension	United Arab Emirates	68%

CVD = Cardiovascular disease, HIV = Human Immunodeficiency Virus, WHO = World Health Organisation, COPD = Chronic Obstructive Pulmonary Disease.

1.11 Non-Adherence to Cardiac Medication in Developed and Developing Countries

While the prevalence of chronic diseases such as cardiovascular disease is increasing internationally, management remains suboptimal at least in part, because patients do not adhere to medications. Studies of the rates of adherence to medications among patients with diverse cardiac diseases return mixed results. Non-adherence to prescribed medications has been reported as a common issue worldwide, with rates ranging from 0% to 100% (Haynes et al. 2008). Cardiovascular medications are key elements in secondary prevention strategies for treating CVD (Australian Institute of Health and Welfare 2017), but improving long-term outcomes requires collaboration between inpatient and outpatient settings (Mathews et al. 2018).

CVD medications have been demonstrated to achieve significant morbidity and mortality benefits, including various cardiac medication classes (Levy et al. 2018). However, despite evidence of the effectiveness of prescribed medications to manage CVD symptoms, non-adherence rates for these drugs have been reported to range from 44.4% to 61%, within and between countries (Paradkar & Sinha 2017) (see Table 1.2 for summary of data from studies in the last decade). Self-reported non-adherence to medication recommendations has been significantly linked to unfavourable outcomes and increased healthcare cost, particularly in patients with CVD (Gehi et al. 2007), and as a contributor to increased rates of rehospitalisation (Riles et al. 2014). Non-adherence in patients with CVD in Spain has been reported at 8% for angiotensin-converting-enzyme (ACE) inhibitors (Ignacio et al. 2017). Another study from Spain indicated that adherence rates among low-income patients with acute coronary syndrome are poor for various treatment classes such as antiplatelet drugs (84.2%); beta-blockers (88.5%);

ACE inhibitors (90.7%) and statins (83.2%) (González López-Valcárcel et al. 2017). In Australia, non-adherence to statin therapy ranges between 23% and 60% of patients in the first year of therapy (Australian Institute of Health and Welfare 2007); unsatisfactory adherence has also been found in elderly Australian patients with CVD in between 2010 and 2014, shown to range between 14% and 43% (McKenzie et al. 2015).

Several of these studies (Australian Institute of Health and Welfare 2007, McKenzie et al. 2015, Ignacio et al. 2017) reveal the rapidity with which some patients stop adhering to medication regimes. At discharge, patients with CVD are at high risk for developing cardiac-related complications; yet once discharged, CVD patients tend to discontinue some cardio-protective medications, particularly beta-blockers, ACEI/ARB and statin (Ho et al. 2009). Mathews et al. (2018)) found that non-adherence rates in US patients discharged from hospital with beta-blockers, statins and ACEI/ARB medications, ranged from 25–31% in the first month, 31–45% in the second month, and 31–33% in the third. Patients with CVD had low persistent use of beta-blockers (at 33%), ACEI/ARB (at 27%), and lipid-lowering agents (at 33%) (Allen LaPointe et al. 2011). Adherence to cardioprotective medications was low in patients with coronary artery disease (CAD) at only 40.7% (Marcum et al. 2013), 66.8% in patients with ACS (Zhu et al. 2011, Nordstrom et al. 2013), and 63% in patients with heart failure (Hood et al. 2018). Adherence to ACEI/ARB was reported to be only 42% in patients with CVD one year after hospital discharge (Winkelmayer et al. 2008), and 50% at two years (Akincigil et al. 2008). Persistence with medications among patients with heart failure in Denmark at five-years was 79% for renin-angiotensin inhibiting drugs, 65% for beta-blockers, 56% for spironolactone, and 83% for statins, using individual-level linkage of nationwide registers (Gislason et al. 2007) (Table 1.2). These figures indicate high risk in these patients of developing cardiac-related complications post-discharge, and hence the importance of developing and applying strategies to promote adherence to cardiac medication regimes (Chen et al. 2015).

This dismaying pattern is repeated in developing countries. In Middle Eastern countries, a cross-sectional study from Lebanon demonstrated medium/low adherence to antihypertensive medication in 49.5% of patients (Yassine et al. 2016). Non-adherence to antihypertensive medications in Saudi patients was reported at 72% (Al Solami 2016). A cross-sectional survey using the 4-item version of the MAQ scale found that patients aged 65 years and over reported high adherence to cardiac medication in China at 75% (Wang et al. 2014). Among studies of developing countries, cross-sectional surveys conducted in the Middle East in patients with hypertension found non-adherence rates were 25.9% in Egypt (Youssef & Moubarak 2002) and 45.6 in the UAE (Bader et al. 2015). Various rates of non-adherence have been reported in patients with cardiac diseases from other developing countries, including 49.6% in India (Dennis et al. 2011), 58.6% in Ghana (Obirikorang et al. 2018), 54% in Iran (Moharamzad et al. 2015), 64.7% in Pakistan (Saleem et al. 2011), 31% in Tunisia (Ben et al. 2006), and 33% in Brazil (Castro et al. 2007). Rates varying from 11% in Nigeria (Akpa et al. 2005), 26.4% in Kazakhstan (Nugmanova et al. 2008) and 39.6% in Iran (Hadi & Rostami 2004) have also been reported.

The estimates of prevalence of cardiac medication non-adherence rates vary enormously in these studies, depending not only on the target patient population and cardiac medication classes, but also the assessment methods employed. Hyre et al. (2007)) utilised a telephone questionnaire including an 8-item version of the Medication Adherence Questionnaire (MAQ) and found that 28.4% of patients with hypertension from the United States had poor adherence to antihypertensive medications. Shalansky and colleagues (2004) also utilised a MAQ scale and found 13% of Canadian patients had poor adherence to cardiovascular medication. A self-reported survey found that 39% of patients with heart failure stopped taking their cardiac medications at six and twelve months after discharge (Newby et al. 2006). Rieckmann et al. (2006)) assessment of medication adherence by electronic medication monitoring and found that 37% of patients with CVD had low levels of adherence. Viana et al. (2014)) used a medication event monitor system and found that patients with heart failure in Portugal were highly adherent to medications, at 97.3% for Acetaminophen, 97.2% for beta-blockers, and 96% for loop diuretics. Two studies from Spain used the proportion of days covered (PDC) to assess medication adherence in patients with CVD and found rates of 69.9% for antiplatelet drugs, 43.3% for beta-blockers, 45.4% for angiotensin antagonists, and 58.8% for statins (Sanfélix-Gimeno et al. 2013). In France, non-adherence to evidence-based cardiac medications measured by the proportion of days covered (PDC) by filled prescriptions was 50% in patients with myocardial infarction (MI) (Tuppin et al. 2010). Studies from Canada demonstrated that the proportion of patients refilling cardiac medications in line with their prescriptions were 57% for statins, 77% for beta-blockers, 30% for calcium channel blockers (CCB) (Rasmussen et al. 2007), and 74% for combined cardiac medications at four months after hospitalisation for MI (Jackevicius et al. 2008). The rates of nonadherence to polypharmacy based on pill counts was lower, at 23.5% among patients following MI in Italy (Valeria et al. 2011). The lack of consistency in these studies, all from developed countries, suggests a need for single agreed approach to enable comparison of results.

Table 1.2 Prevalence of non-adherence to cardiovascular medications in developed and developing countries

Author (Year)	Study type	Patients group	Location	Non-adherence rates
Developed Countries				
Hyre et al. (2007)	Cross-sectional Study	Hypertension	USA	28.4%
Van Wijk et al. (2005)	Cross-sectional Study	Hypertension	USA	39%
Novick et al. (2010)	Cross-sectional Study	Heart Failure	USA	39%
Rieckmann et al. (2006)	Cross-sectional Study	CVD	USA	37%
Wie et al. (2004)	Cross-sectional Study	Older Adults	UK	~80%
Tomaszewski et al. (2014)	Biochemical Screening	Hypertension	UK	25%
Bryne et al. (2018)	Cross-sectional Study	Patients with Statin therapy	UK	65%
Tuppin et al. (2010)	Proportion of Days Covered (PDC)	Myocardial Infarction	France	50%
Danchin et al. (2011)	Cross-sectional Study	Myocardial Infarction	France	77%
Gislason et al. (2007)	Cross-sectional Study	Heart Failure	Denmark	56–83%
Viana et al. (2014)	Cross-sectional Study	Heart Failure	Portugal	96–97.3%
Shalansky et al. (2004)	Cross-sectional Study	CVD	Canada	13%
Rasmussen et al. (2007)	Cross-sectional Study	CVD	Canada	30–77%
Jackevicius et al. (2008)	Population-based cohort Study	Acute Myocardial Infarction	Canada	74%
González López-Valcárcel et al. (2017)	Retrospective Cohort Study	Acute Coronary Syndrome	Spain	84.2–90.7%
Sanfélix-Gimeno et al. (2013)	Cross-sectional Study	CVD	Spain	43.3–69.9%
Ferrajolo et al. (2014)	Literature Review	Patients with Statin therapy	Italy	26%
Valeria et al. (2011)	Pill Counts	Acute Myocardial Infarction	Italy	23.5%
Roughead et al. (2010)	Cross-sectional Study	CVD	Australia	72–84%
Harper et al. (2018)	Cross-sectional Study	CVD	New Zealand	24–50%
Developing Countries				
Awad et al. (2017)	Cross-sectional Study	CVD	Sudan	51%
Yassine et al. (2016)	Cross-sectional Study	CVD	Lebanon	49.5%
Al Solami et al. (2016)	Cross-sectional Study	Hypertension	Saudi Arabia	72%
Youssef et al. (2002)	Cross-sectional Study	Hypertension	Egypt	25.9%
Bader et al. (2015)	Cross-sectional Study	Hypertension	UAE	45.6%
Dennis et al. (2011)	Cross-sectional Study	CVD	India	49.6%
Obirikorang et al. (2018)	Cross-sectional Study	CVD	Ghana	58.6%
Moharamzad et al. (2015)	Cross-sectional Study	CVD	Iran	54%
Saleem et al. (2011)	Cross-sectional Study	CVD	Pakistan	64.7%
Ben et al. (2006)	Cross-sectional Study	CVD	Tunisia	31%
Castro et al. (2007)	Cross-sectional Study	CVD	Brazil	33%
Akpa et al. (2005)	Cross-sectional Study	CVD	Nigeria	11%
Nugmanova et al. (2008)	Cross-sectional Study	CVD	Kazakhstan	26.4%
Soliman et al.(2011)	Cross-sectional Study	CVD	Sri Lanka	3–10%
Wang et al. (2014)	Cross-sectional Study	CVD	China	17%

CVD = Cardiovascular Disease

1.12 Factors Influencing Medication Adherence

Medication adherence affects clinical outcomes among patients with heart disease, with non-adherence linked to reduced physical function, higher risk of hospital admission and death (Ruppar et al. 2016). Suboptimal medication adherence is a multidimensional issue, affected by socioeconomic and patient-related factors such as low educational level, knowledge, beliefs, patients' motivation to manage their illness and their life styles (Broekmans et al. 2010). Lack of social support, medication concerns and a vulnerable psychological, cognitive and/or medical status can also play a part (Kronish & Ye 2013). Factors shown to predict medication non-adherence include low self-efficacy, attitudes and beliefs about medications, low perceived behavioural control, perceived barriers, lack of perceived benefits, and lack of social support (Morrison et al. 2015). Patients with concerns about their medications are more likely to report forgetting to take them and to intentionally skip doses (World Health Organisation 2003). Those in poor health and with co-morbidities are less likely to successfully self-administer (Soumerai et al. 2006). Non-adherence may also be age-related (Krueger et al. 2015), although the evidence in support of this is very mixed and shows a variety of differing patterns. Older age patients with CVD have been shown to be at particularly high risk of non-adherence (Valeria et al. 2011); however other studies have indicated that younger patients are more likely to be non-adherent (Lee et al. 2013).

Medication self-efficacy beliefs may also influence the adoption, initiation and maintenance of medication adherence behaviour (Bane et al. 2006), and may be affected by psychosocial factors such as perceived social support and mood (Cha et al. 2008). Exploring emotions and beliefs while supporting self-efficacy may enhance intrinsic motivation, thereby reducing ambivalence toward behaviour change (Riegel et al. 2006). Understanding reasons for poor adherence may provide a basis for novel medication adherence interventions. It is crucial to promote behaviour change by exploring what drives each patient to make changes or maintain the status quo.

1.13 The Problem Statement

Adherence to medications is a serious challenge, particularly for patients with chronic conditions such as cardiac disease, who often need to take multiple medications for long periods (World Health Organisation 2003). Numerous types of cardiac medication are available and have been proven effective for symptom management and slowing the progression of CVD. Multiple long-established and newer medications, such as angiotensin converting enzyme [ACE] inhibitors, β-blocking agents, aldosterone inhibitors, aspirin, statins and warfarin are prescribed to inhibit the progress of the disease and control its symptoms (Albert 2008, Wu et al. 2008). The risk of mortality and morbidity in patients with cardiac disease increases if adherence to prescribed medication is poor (Hope et al. 2004), with non-adherent patients shown to be 2.5 times more likely to be readmitted to hospital than adherent patients (Miura et al. 2001). Approximately 10% of all hospital admissions and 23% of nursing home admissions in the US are related to medication non-adherence (Grocki & Huffman 2007). Medication non-adherence in patients with cardiac conditions has been shown to vary between 33% to more than 50% (**Table 1.2**), contributing to increased numbers of cardiovascular-related Emergency Department (ED) visits, rehospitalisations, poorer health and well-being, augmented healthcare costs and risks of death (Ashton et al. 1995, Munger et al. 2007, Mukhtar et al. 2014). Thus, adherence to medication is an important factor to improve quality of care and reinforce the effectiveness of secondary prevention (Simpson et al. 2006).

Adherence to medication regimes is a health-related behaviour that is amenable to behavioural intervention. Various behavioural and non-behavioural interventions have been developed for this purpose, ranging from simplification of dosing regimes, patient education, and behavioural methods to more complex interventions such as multifaceted interventions (World Health Organisation 2003, National Heart Foundation of Australia 2011, Nieuwlaat et al. 2014). In general, behavioural interventions have been designed to increase medication adherence by focusing, restructuring, and reinforcing specific behavioural customs. An appropriate level of change in behaviours is sought through engagement in positive health behaviours to maximise health benefits (Salamonson et al. 2007). Behavioural interventions have comprised strategies such as motivational counselling, self-monitoring, and phone and mail reminders.

Interventions have also been used in combination, addressing different non-adherence factors so that a combination of strategies may achieve cumulative and synergistic benefit (Ogedegbe et al. 2008, Smith et al. 2008). However, studies of such interventions have often been conducted with mixed samples of patients with chronic diseases, making it difficult to extrapolate conclusions for specific patient groups (Haynes et al. 2005). It is essential to optimise cardiac disease management by enhancing patients' adherence to prescribed medications to improve outcomes. This should be achievable through engaging patients in positive behaviour change, as combined approaches such as behavioural intervention with education and/or reminders have shown promising results in different patient populations (World Health Organisation 2003, Salamonson et al. 2007). It is recommended that nurse-led intervention can enhance adherence to cardio-protective medications through addressing the principle behavioural causes of sub-optimal adherence such as patients' ability to correctly self-administer and refill medications and their beliefs about medication (Al-Ganmi et al. 2019). Nurses can fill significant treatment gaps in the management of risk factors for patients with CVD as nurses have unique roles in cardiac care to meet the needs of these patients (Jiang et al. 2007). Nurses have the primary role in providing case management to not only reduce the risk factors of CVD but also to promote adherence to treatment guidelines and protocols, to minimise rehospitalisation, morbidity and mortality in patients with CVD (Hayman et al. 2015).

1.14 The Significance of the Study

CVD is a leading cause of death worldwide and responsible for one death every 12 minutes in Australia (Australian Bureau of Statistics 2014); despite improvements in recent decades it remains one of Australia's biggest health problems and burdens on the healthcare system. To optimise care for these patients and reduce the disease burden, it is essential that these patients are managed appropriately.

Management of CVD often includes prescription of complex medication regimes to prevent and/or delay disease progression, control symptoms, and improve survival. Survival from myocardial infarction has improved remarkably over the last two decades, mainly due to advances in cardiovascular medications and interventional cardiology which have contributed to reduce fatal events (Rashid et al. 2014). These medications have substantially improved survival and extended life expectancy of patients with myocardial infarction with increasing numbers of patients surviving to live with chronic CVD (Rashid et al. 2014). However, patients with CVD are at increased risk of new non-fatal and fatal vascular events after hospital discharge compared to individuals without such history (Sol et al. 2011). Newer and complex cardiovascular medication regimes are increasingly prescribed to prevent and/or delay CVD progression, control symptoms, and improve survival. The risk of recurrent cardiac events is affected by medication non-adherence, which is associated with significant but often unrecognised cardiovascular risk (Ho et al. 2008). Therefore, it is essential that patients with CVD adhere to their medication regime to optimise the effectiveness of medical therapy. It is equally essential that clinicians find effective means to support and enable patients to adhere to their medication regimes, but this knowledge base is currently small and fragmented.

This thesis therefore set out to identify the current evidence for characteristics and interventions that can affect the adherence of patients with CVD to their medication regimes, and to subsequently incorporate this into a trial proposal. This evidence was sought from published literature, and from self-reported characteristics of patients shown to be predictive of medication adherence. To maximise the breadth and diversity of evidence amenable to the study, two countries and two points in the CVD patient journey were chosen for study. Sites were chosen in Australia and Iraq, both countries where CVD is a health priority, but within very different cultural, religious, geo-political, developmental and economical contexts. Hospital in-patients were identified as representative of the acute stages of the CVD patient journey, with patients surveyed about the period immediately prior to their admission. Cardiac rehabilitation was chosen, representing a more stable phase of self-management and community support.

1.15 Aims

The aims of this thesis are to develop a widely applicable, evidence-based nurse-led intervention tailored to address factors predictive of poor adherence to medication regimes in patients with CVD, and to design a protocol to trial this intervention. The study objectives are:

1. To critically appraise and synthesise the best available evidence on the effectiveness of interventions suitable for delivery by nurses, designed to enhance cardiac patients' adherence to their prescribed medications;
2. To identify factors predictive of medication adherence in patients with cardiovascular disease admitted or attending hospital in Australia;
3. To compare factors associated with medication non-adherence in patients with CVD in developed and developing nations (Australia and Iraq);
4. To design a protocol suitable to test the effectiveness of an evidence-based nurse-led intervention in promotion of medication adherence in patients with CVD.

CHAPTER 2 Systematic Review of the Literature

2.1 Introduction of the Chapter

This chapter provides systematic review of the literature on the effective interventions used by nurses to improve cardiac patients' adherence to cardiac medications. This chapter is based on a paper published in the Journal of Advanced Nursing:

Al-Ganmi A.H., Perry, L., Gholizadeh, L. & Alotaibi A.M. (2016). Cardiovascular medication adherence among patients with cardiac disease: a systematic review. Journal of advanced Nursing, 72, 3001–3014. https://doi.org/10.111/jan.13062.

This paper aimed to report various approaches, trialled and suitable for delivery by nurses and effective at improving the adherence of cardiac patients to their prescribed cardio-protective medications. It sought to collect, review and synthesize the best available evidence on the effectiveness of interventions within the nursing scope of practice, designed to enhance cardiac patients' adherence to cardio-protective medications. This paper published in Journal of Advanced Nursing. The published format of this article is provided in (**Appendix L**). This journal was chosen because it seeks to promote the development and exchange of knowledge that is directly relevant to all ranges of nursing practice, and because of the journal's wide range of readership and impact factor of 2.267.

2.2 Background

Cardiovascular disease (CVD) remains the leading cause of mortality among men and women and is responsible for one-third of all deaths worldwide (World Health Organisation 2004). Optimal prescription of cardio-protective pharmacological therapies is estimated to save 80, 000 lives per year in the US (Newby et al. 2006). Consistent use of cardio-protective medications, such as aspirin, β-blocking agents, lipid-lowering therapy, singly and in combination, in patients with heart failure has been associated with substantially improved long-term survival. Long-term adherence to outpatient medications has also been linked to improved long-term outcomes in these patients (Newby et al. 2006).

Cardio-protective medicines are the primary therapy for CHD, but adherence to these medications is suboptimal, resulting in insufficient control of disease symptoms and increased risk of future cardiovascular events, rehospitalisation and death (Baroletti & Dell'Orfano 2010). Adherence to medication recommendations is necessary to receive the full benefits of the medications. Medication non-adherence has been defined as 'taking less than 80% of prescribed doses and can also include taking too many doses' and it is associated with an increased risk of poor health, adverse clinical events and death (Nieuwlaat et al. 2014). It is estimated that up to 50% of patients with CHD in high income countries do not take their medications as prescribed (Laba et al. 2013). Poor medication adherence has been linked to recurrent cardiac events and adverse patient outcomes (Poluzzi et al. 2011, Nieuwlaat et al. 2014). The prevalence of patients in the ageing Australian population who are non-adherent to cardiovascular medications has been reported to range from 14% to 43%, posing a serious barrier to secondary prevention (McKenzie et al. 2015). Thus, long-term medication adherence in Australia remains unsatisfactory, with the situation changing only very slowly (Simons et al. 2011). Poor medication adherence rates undermine the translation of the benefits of well-established evidence-based cardiovascular medicines into practice, reducing the effectiveness of secondary prevention therapies (Haynes et al. 2005). It is crucial that adherence to cardiovascular medicines is optimized to improve disease symptoms and prevent the onset of further serious cardiac events (van Dalem et al. 2012).

The effectiveness of a wide variety of interventions intended to enhance medication adherence in patients with CHD has been trialled. Several diverse and complex behavioural, educational and combined intervention approaches and outcomes measures have emerged; however, the effectiveness of these interventions needs to be carefully evaluated due to the diverse methodologies used in the studies. It is important that healthcare professionals are aware of effective practical strategies and have the necessary skills to translate these interventions to outpatient healthcare settings.

Therefore, behavioural interventions based on patient centred approaches to enhance medication adherence are required to improve patient care, outcomes and treatment costs. Delivery of effective healthcare requires that providers understand factors related to non-adherence and their roles in enhancing medication adherence; that they assess patient adherence and monitor CVD progression and response to treatment.

2.3 Aims of the Systematic Review of the Literature

This review aimed to identify and review studies that examined the effectiveness of interventions amenable to delivery by nurses to improve the adherence of cardiac patients to their prescribed cardio-protective medications.

2.4 Review Methods

A systematic literature search was conducted using six electronic databases: Medline, EMBASE, CINAHL, the Cochrane Library, ProQuest and Web of Science. These databases and Google Scholar were searched for articles published in English between

January 2004–December 2014. The reference lists of all selected articles including review articles were searched for additional studies. The keywords used in the search strategy were based on the 'PICOS' framework (**Table 2.1**). Studies were included if they were primary research reported the results of unconfounded evaluation of interventions suitable for delivery by nurses to increase medication adherence for patients with CHD. The following inclusion criteria were applied:

- Study design was a randomised control trial (RCT), clinical trial or controlled clinical trial that examined the effectiveness of an intervention to increase adherence to medications among patient with cardiac disease, used for secondary prevention or treatment of cardiac disease, where an intervention group was compared with a control group who received standard care or a clearly justified comparison group;
- The population of interest comprised male and female adults (≥18 years old) with a diagnosis of a cardiac disease;
- The intervention strategy was suitable (within the scope of practice) for delivery by nurses and had either a primary or secondary aim to increase the adherence to medication of patient with cardiac disease;
- Patients were followed up for at least 6 months;
- Medication was self-administered, that is, was not administered by a healthcare professional or carer and measured by any method e.g.: pill count, electronic monitoring, refill or prescription records or self-reported data.

Table 2.1 PICOS Framework (Criteria for considering studies)

Criteria (PICOS)	Keywords
Population (P)	Cardiovascular disease* or Coronary Artery Disease* or Coronary Heart Disease* or Acute Coronary Syndrome or Myocardial infarct* or Myocard* Isch* or unstable Angina or Myocard* or cardiac* or Cardiac patients or Blood pressure.
Intervention (I)	Behavio* change intervention or behavioural change or nursing intervention or behavio* (change, enhance*, reinforce) or counselling or medication (educat*, counsel*, intervene*) or nurse-led intervention or nurse-led or nurse councel* or motivational interview or self-management or self-efficacy or cardiac treatment (statin*, antiplatelat*, aspirin, antilipid, β-blockers, blood pressure (BP) medication).
Control or comparison (C)	A separate group who received standard care or a clearly justified comparison (no specific keywords)
Outcome (O)	Medication adherence (increase*, enhance*, improve*, intensify*, reinforc*, promot*) or treatment adherence or medication compliance or medication concordance.
Study type (S)	Randomised Controlled Trial (RCT) or clinical trial or controlled clinical trial or random allocation or double-blinded method or single blinded-method or (random$ and placebo$).

Studies were excluded if they recruited patients following cardiac surgery. Following cardiac surgery patients are commonly newly started on medications. Post-operative patients are a vulnerable group with high medication self-management burden, and their prescription regime is often new, and they may have no history of medication adherence. Their medication regimes may be compounded, particularly in the early period post-surgery, by additional non-cardiac medications such as analgesics and anticoagulants. It is reasonable to claim that their new and more complex medication regimes pose additional challenge. Studies were also excluded if they were written in a language other than English; included non-cardiac disease patients; tested interventions that required delivery by a non-nursing healthcare professional, e.g. pharmacist; were conducted in inpatient settings; and had less than 6 months follow-up, because cardiovascular medications typically require long-term adherence.

2.5 Search Outcomes

In total, search strategies identified 1962 citations of potential relevance. Initial screening of study titles and abstracts revealed that more than 95% of the retrieved studies did not meet the review inclusion criteria, leaving 94 papers for further evaluation. The full texts of these papers were then reviewed, and 14 studies were retained for assessment. The flow of studies through the selection process is summarised in **Figure 2.1**.

2.5.1 Quality Appraisal and Data Abstraction

The quality of included studies was appraised by the principle investigator, the student, using the Cochrane Collaboration tool for assessing the risk of bias (Higgins et al. 2011). The study supervisors assessed the accuracy of the first appraisals independently and provided feedback. Discrepancies were resolved by discussion (**Figure 2.2**). Data were extracted and analysed using a predefined form. After quality appraisal of these studies, 14 were retained for the review. Details of data extracted are available in **Appendix A**.

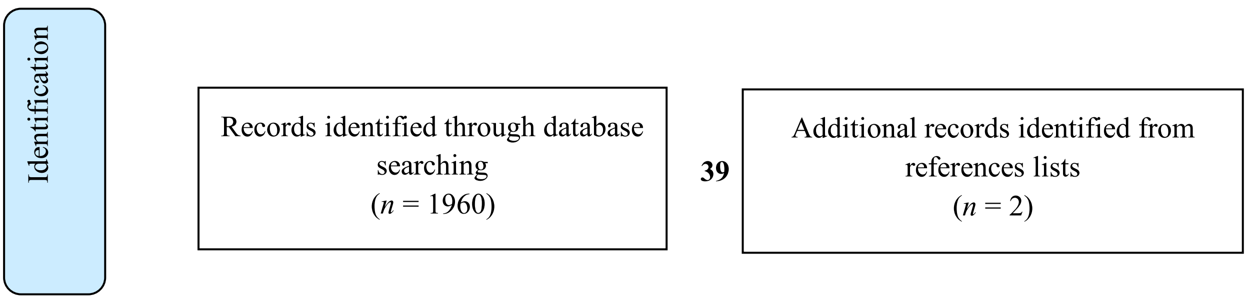
2.6 Synthesis

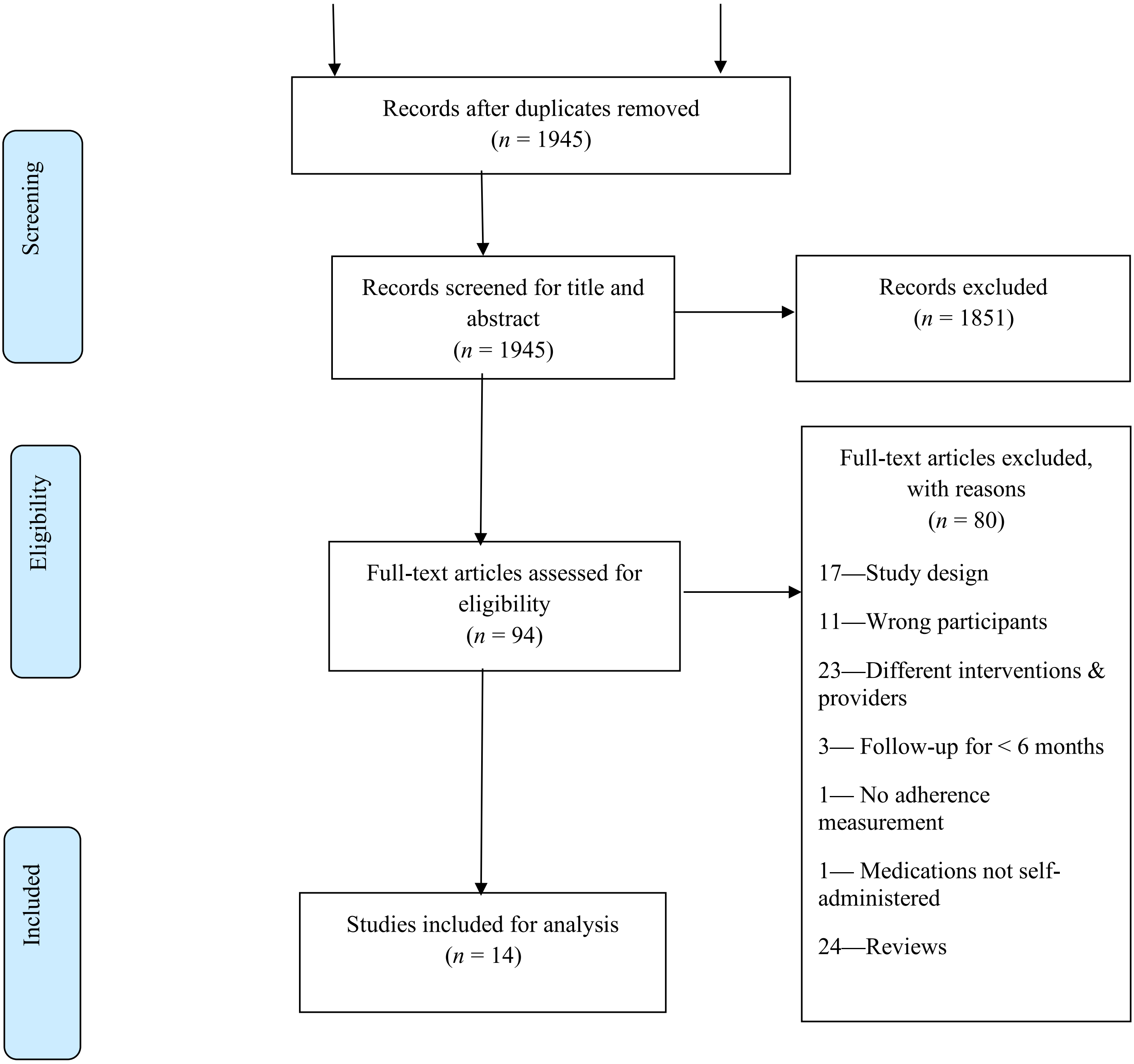
Multiple sources of heterogeneity (interventions, adherence measures and outcomes) were observed across the included studies; formal meta-analysis was therefore not appropriate. The heterogeneity was explored qualitatively by comparing the characteristics of included studies. Studies were grouped according to the main components of the interventions (**Appendix B**).

2.7 Results

These fourteen included studies contained data on 4,548 patients with cardiac disease. These studies were summarised based on the country of origin, participants' cardiac disease diagnostic group and the practice setting of interventions (**Table 2.2**). None of these studies detailed or considered the potential effect of socio-demographical, literacy or economic characteristics on intervention outcomes. The median follow-up time was 1 year, ranging from 6 months to 24 months. Most studies achieved their endpoint outcomes at 3–9 months. Interventions varied, with single, combined and multifaceted component parts. Interventions and study characteristics are detailed in **Appendix B**.

Figure 2.1 PRISMA Flow Diagram




Screening
Eligibility
Included
Records after duplicates removed
(n = 1945)
Records screened for title and abstract
(n = 1945)
Records excluded
(n = 1851)
Full-text articles assessed for eligibility
(n = 94)
Full-text articles excluded, with reasons
(n = 80)
17—Study design
11—Wrong participants
23—Different interventions & providers
3— Follow-up for < 6 months
1— No adherence measurement
1— Medications not self-administered
24—Reviews
Studies included for analysis
(n = 14)

2.7.1 Risk of Bias Assessment

Risk of bias was assessed using the Cochrane Collaboration tool (Higgins et al. 2011) for selection, performance, attrition, detection, reporting and systematic bias. All trials provided information about adequate sequence generation, 10 studies described the measures used to blind outcome assessors from group allocation. Four studies avoided performance bias (Jiang et al. 2007, Ogedegbe et al. 2008, Beune et al. 2014, Leiva et al. 2014) by providing information about adequate blinding of participants and personal. Ten studies reported participants lost to follow-up; six trials provided study protocols and reported the methods of outcomes assessment (medication adherence). The remaining studies reported all outcomes but without study protocols (Schroeder et al. 2005, Jiang et al. 2007, Ogedegbe et al. 2008, Smith et al. 2008, Guirado et al. 2011, Kripalani et al. 2012, Rinfret et al. 2013, Leiva et al. 2014) (**Figure 2.2**). GRADE was used to rate the quality of evidence for medication adherence. Scores ranged –1 or +1 and were summed to produce overall scores (4 = high, 3 = moderate, 2 = low and 1 = very low) based on the risk of bias, design, inconsistency, indirectness and imprecision in their scores (EPOC Resources for review authors 2013). Most studies were at low or unclear risk of bias and the quality of evidence was rated moderate for the outcomes (**Figure 2.2**). Hence, study results should be interpreted with caution.

Table 2.2 General characteristics of included studies

COUNTRY OF ORIGIN	UNITED STATES	UNITED KINGDOM	NETHERLANDS	CHINA	CANADA	SPAIN	TURKEY
	4 studies Ho et al. 2014 Kripalani et al. 2012 Ogedegbe et al. 2008 Smith et al. 2008	2 studies Schroeder et al. 2005 Wald et al. 2014	2 studies Beune et al. 2014 Nieuwkerk et al. 2012	2 studies Jiang et al. 2007 Ma et al. 2014	1 study Rinfret et al. 2013	2 study Guirado et al. 2011 Leiva et al. 2014	1 study Hacihasanoğlu & Goözuöm 2011

PARTICIPANT DIAGNOSTIC GROUP	Hypertension	Coronary Heart Disease	Myocardial infarction	Acute Coronary Syndrome	Undefined; on lipid-lowering drugs
	8 studies Beune et al. 2014 Guirado et al. 2011 Hacihasanoğlu & Goözuöm 2011 Leiva et al. 2014 Ma et al. 2014 Ogedegbe et al. 2008 Schroeder et al. 2005 Wald et al. 2014	2 studies Jiang et al. 2007, Kripalani et al. 2012	1 study Smith et al. 2008	2 studies Ho et al. 2014 Rinfret et al. 2013	1 study Nieuwkerk et al. 2012

PRACTICE SETTING	Primary care	Out-patient clinics	Community health centres	Dept. of Veterans Affairs Medical Centre
	8 studies Beune et al. 2014 Guirado et al. 2011 Hacihasanoğlu & Goözuöm 2011 Jiang et al. 2007 Kripalani et al. 2012 Leiva et al. 2014 Ogedegbe et al. 2008 Wald et al. 2014	3 studies Nieuwkerk et al. 2012 Schroeder et al. 2005 Smith et al. 2008	2 studies Ma et al. 2014 Rinfret et al. 2013	1 study Ho et al. 2014

Figure 2.2 Methodological quality summary: review authors' judgements of each methodological quality of each included study

	Random Sequence Generation (Selection Bias)	Allocation concealment (Selection Bias)	Blinding of participants and personal (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (Attrition bias)	Selective reporting (reporting bias)	Group balance at baseline	Intention to treat analysis conducted	Groups receive same treatment (a part from the intervention)
Beune et al. (2014)	+	+	-	+	+	+	+	+	+
Guirado et al. (2011)	-	?	-	-	+	?	+	+	+
Hacihasanoğlu & Goözuöm (2011)	-	-	-	+	+	+	+	-	+
Ho et al. (2014)	+	+	?	+	+	+	+	+	+
Jiang et al. (2007)	+	?	+	+	+	?	+	+	+
Kripalani et al. (2012)	+	+	-	+	-	?	+	+	+

Leiva et al. (2014)	+	+	+	+	+	?	+	+	+
Ma et al. (2014)	+	-	-	-	+	+	+	-	+
Nieuwkerk et al. (2012)	+	?	-	?	?	+	+	+	+
Ogedegbe et al. (2008)	+	+	+	+	+	?	+	+	+
Rinfret et al. (2013)	+	+	-	+	+	?	+	+	+
Schroeder et al. (2005)	+	+	-	+	?	?	-	+	+
Smith et al. (2008)	+	+	?	+	+	?	+	+	?
Wald et al. (2014)	+	?	-	-	?	+	+	-	+

2.7.2 Medication Adherence Measurement

Methods for measuring and monitoring medication regime adherence varied in these trials. Six studies each measured adherence by self-report (Jiang et al. 2007, Guirado et al. 2011, Hacihasanoğlu & Goözuöm 2011, Nieuwkerk et al. 2012, Beune et al. 2014, Ma et al. 2014) and by pharmacy refill electronic data (Smith et al. 2008, Rinfret et al. 2013, Ho et al. 2014, Leiva et al. 2014, Wald et al. 2014). The Medication Event Monitoring System (MEMS) pill bottle caps was used in one study (Schroeder et al. 2005) and two studies applied both self-report and MEMS (Ogedegbe et al. 2008, Kripalani et al. 2012).

2.7.3 Type of Intervention

Interventions were categorised according to their prominent components and included: (1) multifaceted; and (2) behavioural and educational interventions. The latter comprised: (a) text message and mail message; (b) telephone calls; (c) motivational interviewing; and (d) nurse-led counselling and education. To determine the amenability of an intervention to be nurse-led, it is important to consider the formal descriptions, definitions, systems and scope of nursing practice operational in the nurses' country and field of practice. Nurse-led interventions can be assessed by comparison to this nursing scope of practice, as routinely stated by national nursing bodies; and by considering the feasibility of these interventions to be led by nurses, in this case, within cardiac care settings. The complex nature of some interventions made them difficult to categorize, but this was based on the main component of intervention. Three studies examined text message (TM) and/or mail message interventions (Smith et al. 2008, Kripalani et al. 2012, Wald et al. 2014); two studies tested multifaceted intervention strategies (Ho et al. 2014, Leiva et al. 2014); two studies investigated the effect of structured telephone calls (Hacihasanoğlu & Goözuöm 2011, Rinfret et al.

2013) and two studies used the motivational interviewing approach (Ogedegbe et al. 2008, Ma et al. 2014). Five interventions were classified as nurse-led counselling and education (Schroeder et al. 2005, Jiang et al. 2007, Guirado et al. 2011, Nieuwkerk et al. 2012, Beune et al. 2014). The heterogeneity of interventions, measurement tools and methods precluded meta-analysis of baseline and post-intervention rates of adherence for the reviewed studies.

2.7.3.1 Multifaceted Interventions

The effectiveness of multifaceted interventions for enhancing medication adherence was described and evaluated by two studies. Ho et al. (2014) used a four-stage multifaceted intervention that entailed: medication reconciliation and tailoring, education about medications, collaborative care and two types of scheduled voice messaging (educational and medication refill reminder calls). Similarly, Leiva et al. (2014)) evaluated a multifaceted intervention incorporating motivational interviewing, pillbox reminders, family support, blood pressure measurements and antihypertensive reminder forms and simplification of dosing regimes in patients with hypertension. Ho et al. (2014) found that adherence rate improved at 12 months follow-up by 89.3% in the intervention arm compared with 73.9% with usual care for four classes of medications. On the other hand, Leiva et al. (2014)) found no significant between groups differences in antihypertensive adherence at 12 months (514% vs. 508%)

in intervention and control groups respectively (**Appendix B**). The Ho et al. (2014)) study was high quality; however, Leiva et al. (2014)) did not employ a blinding process and delivery of the intervention by nurses varied according to their characteristics and the methods of delivery, possibly resulting in overestimation of the intervention effect (**Appendix B**). Overall, this type of intervention approach appeared likely to increase adherence to medications after hospital discharge post ACS and was costed at $360 per patient per year (Ho et al. 2014).

2.7.3.2 Text and Mail Message Interventions

Three studies assessed the effectiveness of text message (TM) (Wald et al. 2014) and mail message reminders (Smith et al. 2008, Kripalani et al. 2012). In the Wald et al. (2014)) study, participants in the intervention group received automatically generated daily TM reminders which questioned patients whether they had taken their blood pressure and/or lipid-lowering medications; whether the message had reminded them to take it; if they had forgotten or whether they had simply not taken it. This study showed 16% improvement in medication adherence (95% CI 7–24%, P < 0001) at 6 months follow-up and a statistically significant difference between groups of patients who had stopped medication completely and those who continued to take <80% of the prescribed regime (**Appendix B**). However, participants' high adherence rates at baseline and unclear randomization and blinding procedures may have resulted in under or overestimation of intervention effects (**Appendix A**). Two studies applied a less individual approach, one mailed graphical postcards focusing on refill and other important reminders to patients with CHD (Kripalani et al. 2012), another focused on improving cognitive aspects of medication adherence by sending two letters to patients and to primary care providers describing the importance of beta-blockade (Smith et al. 2008). Kripalani et al. (2012)) showed a non-significant difference in improvements in adherence between groups (329% vs. 329% respectively), whereas the Smith et al. (2008)) study improved adherence rates among patients in the intervention group by 17%, increasing the days covered to 80% in this group (relative risk = 117; 95% CI = 102–129; P = 004). The quality of Smith et al. (2008)) study was good in terms of randomization methods, intervention and strategies used for applying the intervention and follow-up. By contrast, graphical mailed refill reminders failed to improve medication adherence, attributed to quality issues with randomization and blinding processes (**Appendix A**). Overall, the TM and mail message approaches appeared potentially effective and feasible strategies as reinforcement for taking medication and improving medication adherence.

2.7.3.3 Telephone Call Interventions

Two studies (Hacihasanoğlu & Goözuöm 2011, Rinfret et al. 2013) examined the use of structured phone calls with interactive components to improve medication adherence. Hacihasanoğlu & Goözuöm (2011)) randomly allocated patients with hypertension to three groups to receive a 6-month nurse-based medication educational intervention alone, educational intervention plus home monitoring for medication adherence, or a control group. Both intervention groups received monthly follow-up phone call interviews providing them with information about hypertension. Similarly, in the Rinfret et al. (2013)) study, patients with dual antiplatelet therapy (DAT) (n = 150) were randomised to either nurse phone calls in 1 week and then at 1 month, 6 months and 9 months to assess adherence, reinforce optional drug compliance and discuss the factors affecting adherence or to a control group (**Appendix A**). Both studies showed a statistically significant increase in medication adherence using different measures. At 10 months follow-up, there was a statistically significant increase in regular medication intake ratios after education in groups A and B (80%, 85%, respectively, P = 0001) but not in the control group (42%, P > 005) (Hacihasanoğlu & Goözuöm 2011). Combined education (group B) was shown to have a more positive effect on adherence self-efficacy than education alone (group A) and no intervention (control group) (72.27 (SD= 5.27); 71.10 (SD= 6.42); 56.85 (SD= 6.10) respectively, F = 83.131; P = 0001) (Hacihasanoğlu & Goözuöm 2011). The Rinfret et al. (2013)) study showed that participants in both groups had high adherence to antiplatelet drugs at 12 months, with 99.2% (ranging from 97.5–100%) of the intervention group taking aspirin compared with 902% (ranging from 84.2–95.4%) of the control group; clopidogrel, 99.3% (ranging from 97.5–100%) in the intervention group vs. 91.5% (85.1–96.0%) % in the control group, (p < 00001). However, the study results may have been biased by the lack of blinding of patients and intervention providers, although it was impractical in this study (**Appendix A**).

2.7.3.4 Motivational Interviewing Strategies

Motivational interviewing has been used as an approach to increase adherence to medication in cardiac patients. Ogedegbe et al. (2008)) conducted a randomised controlled trial in two community-based primary care practices in the US, evaluating the efficacy and effects of practice-based motivational interview (MINT) counselling on medication adherence and blood pressure in 190 African American patients with hypertension. Based on intention-to-treat analysis using mixed-effects regression, the MINT group achieved a higher MEMS adherence rate at 12 months follow-up compared with the control group (57% vs. 43% respectively, P < 005), with an absolute between-group difference of 14% (95% CI, –0.2 to –27%). The MINT group received behavioural counselling about medication adherence for 30–40 minutes at 3, 6, 9 and 12 months, which led to steady maintenance of medication adherence over 12 months, while adherence rates declined overtime in the control group. Similarly, Ma et al. (2014)) applied MINT counselling, based on social cognitive theory, to 120 patients with hypertension from two community health centres in China. This intervention entailed strategies to promote adherence to behaviour changes, summarising the pros and cons of proposed behaviour changes, setting realistic and specific goals for behaviour modification and prompting patients to follow plans for behaviour change

(**Appendix A**). Adherence to medication was improved in the MINT counselling group compared with the control group at 6 months follow-up (29.72 (SD = 3.46) vs. 25.30 (SD = 3.11)) respectively, (t = 0.039, P = 0.034). Mean scores for medication adherence were increased within-groups with mean difference between baseline and 6 months for intervention group of (23.25 (SD = 3.02); 29.72 (SD = 3.46)) respectively, (t = 0.039, P = 0.034) and (22.13 (SD = 2.89); 25.30 (SD 3.11)) (t = 0. 039, P = 0.061) (**Appendix A**). This form of MINT was theory– based and shown to be effective using accepted valid measures for adherence assessment over longer duration of follow-up.

2.7.3.5 Nurse-Led Counselling and Education

Five studies intended to improve medication adherence using behavioural interventions and education through nurse-led counselling. Four studies demonstrated no or little evidence of effect (Schroeder et al. 2005, Jiang et al. 2007, Guirado et al. 2011, Beune et al. 2014). These results may be attributed in part at least to feature of the research methods, such as self-selected populations with high adherence levels at baseline (Schroeder et al. 2005) and randomisation and blinding processes bias (Jiang et al. 2007, Guirado et al. 2011, Beune et al. 2014) (**Appendix A**). Nieuwkerk et al. (2012)) revealed that adherence to lipid-lowering medication increased from 95% to 100% in the intervention group and from 90% to 95% in the control group. At 18 months follow-up, the intervention group had higher adherence to statin therapy than the control group (9.39 (SD 0.15) vs. 8.86 (SD 0.15)) respectively, with an absolute difference between groups of 0.53 (0.02–1.05), (r = –0.36, P < 0.01) (**Appendix A**). With 201 patients on statin therapy randomised to receive nurse-led multifactorial cardiovascular risk-factor counselling or standard care, statistically significant outcomes were attributed to the more extensive personal contact with the nurse practitioner and risk-factor counselling in the intervention group compared with the control group. Overall, most studies demonstrated no improvement in outcomes from nurse-led behavioural interventions (Schroeder et al. 2005, Jiang et al. 2007, Guirado et al. 2011, Beune et al. 2014), while the Nieuwkerk et al. (2012)) study appeared to offer an opportunity to improve medication adherence. However, taking into consideration the baseline difference between groups, these study findings should be interpreted with caution.

2.8 Discussion

This review of interventions to enhance adherence to medications in cardiovascular care highlighted not only the varying effectiveness of approaches trialled but also the varying methods of evaluation. The evidence of effectiveness presented for these interventions was inconsistent, due at least in part to the different cardiac disease populations and adherence measurement methods used in these studies. Results were not materially affected by age, sex or smoking (Wald et al. 2014), but the impact of socio-economic status could not be determined; however, examination of the effect of these factors went beyond the review research question (Jiang et al. 2007).

Motivational interviewing, either alone or combined with another adherence approach such as phone or text message education and reminders, appeared the most promising behavioural intervention for improving medication adherence, with potential for wide application across patients with different forms of cardiac disease. Interventions that used motivational interviewing (MINT) strategies were successful at maintaining medication adherence over time among hypertensive patients (Ogedegbe et al. 2008). The results support those of previous studies, demonstrating that MINT may be a useful approach for addressing medication adherence (DiIorio et al. 2008), because it enhance patient readiness to change, increase their confidence in their ability to overcome barriers and increase self-motivation to achieve desired outcomes (Rollnick & Miller

1995). This approach entailed setting realistic and specific goals for behaviour modification and prompted patients to follow their plan for behaviour change. This can be achieved when trained nurses integrate adherence behaviour into patients' daily routines and reinforce the positive effect of MINT by follow-up using phone calls, text messaging or mails as a mean of multifactorial intervention.

Multifaceted interventions also demonstrated statistically significant improvement in medication adherence (Ho et al. 2014). Study findings were consistent with other successful multifaceted interventional studies, which have included medication review with a specific focus on regime simplification (Bernsten et al. 2001), individualised patient education combined with medication reminders (Hawe & Higgins 1990), or a dose administration aid (Lee et al. 2006). These results also accorded with a study (Edworthy et al. 2007) that found statistically significant improvement in adherence for both beta-blocking and lipid-lowering agents with counselling by nurses and pharmacists along with video, printed material and phone follow-up. Multifaceted interventions have broadly demonstrated promising results, but make it difficult to draw conclusions in favour of any particular combination of interventions or intensity because of the heterogeneity and complexity of interventions, compounded by multiple adherence measures (Topinková et al. 2012) and drug classes (van Eijken et al. 2003). The cost of these interventions is also an important consideration for roll-out, this could not be determined as interventions were not described in sufficient detail.

A common element of many medication adherence interventions was education. However, the methods of delivering education differed and outcomes were inconsistent. Effective nurse-based medication educational interventions included 6-monthly face-to-face education sessions (Hacihasanoğlu & Goözuöm 2011) about the important of regular medication taking, medication efficacy, possible side effects and the importance of follow-up visits. Medication education was also successfully combined with automatic voice message reminders at 1 week and 1 month after hospital discharge for 12 months (Ho et al. 2014). By contrast, written medication educational materials delivered by a nurse combined with three structured counselling sessions was not associated with statistically significant improvement in medication adherence (Guirado et al. 2011, Beune et al. 2014).

Comparisons across assessments of adherence were also difficult. The medication event monitoring system (MEMS), one of the most reliable objective assessment methods was expensive and not readily available for some dose forms (Remington et al. 2007, van den Boogaard et al. 2011). Subjective self-reporting measures are commonly used as they are relatively simple and less expensive; a number are well-validated and have been strongly correlated with objective measures of adherence in different populations (Nguyen et al. 2014).

For text and mail message interventions, studies showed similar improvements in medication adherence, at 16% (Wald et al. 2014) and 17% (Smith et al. 2008), respectively. These findings are consistent with recent RCTs reporting that bidirectional text messages resulted in statistically significant improvement in anti-retroviral treatment adherence among patients with Human Immunodeficiency Virus (Lester et al. 2010) and with hypertension (Márquez Contreras et al. 2005). Similarly, phone call interventions significantly improved adherence self-efficacy to antihypertensive medications at 10 months follow-up when combined with health promotion theory-based medication education and behavioural modification targeting patients' lifestyles (Hacihasanoğlu & Goözuöm 2011). Cutrona et al. (2010)) review concluded that phone calls both by trained lay people and by a nurse yielded statistically significant improvements in cardiovascular adherence. Likewise, tailored telephone call nursing interventions reduced the time commitment, the cost for the care provider, provider costs and improved medication adherence for patients with chronic diseases (Bosworth et al. 2009). However, a review by Mansoor et al. (2013)) found that informational interventions had little or no impact on improving medication adherence. This could be due to how well healthcare providers delivered the interventions, the patient groups, study design and differences in the relative contribution of each element to the intervention. For example, information supplied passively to the patient may not be adequate and the additional element of requiring a response from the patient may be what was responsible for statistically significant change. All in all, using technology in the form of phone message intervention provided by nurses appeared feasible, cost-effective and likely to be an effective tool to improve medication adherence in resource-limited settings.

The results of nurse-led interventions were mixed although one study (Nieuwkerk et al. 2012) was successful in increasing adherence rates for lipid-lowering medications by enhancing patients' knowledge through structured counselling sessions. A similar intervention was shown to be beneficial in patients with hypertension (Logan et al. 1983). Nurse-led interventions have also failed to show positive effects on medication adherence in other populations. For example, Clarke et al. (2002)) found no significant between-group differences in mean change scores of medicine taking after 12 months of a nurse-led diabetes management programme. However, overall, the evidence is not adequate, with current studies limited by short follow-up, small sample size and inconsistent adherence measures.

To date, of nurse-delivered interventions to improve adherence to cardiovascular medications, multifaceted interventions appear to offer the best opportunities to optimize medication adherence, with component behavioural interventions in the form of motivational interviewing, educational content, text and/or phone messaging showing the greatest success.

This review has some limitations. All papers reviewed were from English-language sources and published since 2004; study results may not represent less contemporary non-English publications. The wide variety of medication adherence measurement methods used in these studies made it difficult to detect changes in adherence to medications, although, most studies did use validated self-report questionnaires. Finally, the lack of concealment of randomisation allocation, blinding, self-reporting bias and high rate of participant dropout in some studies could compromise the integrity of the study data. Hence, for each study, we examined potential biases that might explain differences among studies.

2.9 Conclusion

With the rapidly rising prevalence of CVD worldwide, new and complex medication regimes are emerging which challenge both patients and healthcare providers (Hauptman 2008). Of the interventions intended to improve adherence to cardiovascular medications tested by studies in this review, multi-component interventions, tailored to address the patients' health behaviours, appeared to offer most promise. Combined interventions (i.e. using a combination of strategies) need to be detailed and employ multiple approaches such as motivational interviewing and education that target the desired behaviour change and reinforcement of these behaviours such as with phone or text message strategies. However, while this review provides pointers for promising intervention approaches available to nurses, further studies are required to develop and test ways to accommodate these promising interventions in daily practice. It is imperative that interventions chosen are theory-based and evaluated in robust trials to demonstrate effects on clinical outcomes, feasibility in usual practice settings and sustainability. There is clearly a future role for technology in automating management of, for example, text and mail messaging. Healthcare providers in primary and secondary health settings should maximize the health benefits offered by medications by adopting those strategies shown to be effective at enhancing patients' adherence to their medications. Researchers should clearly justify and specify methodologies to generate a cumulative body of knowledge that can be used to inform clinical practice. Further investigation of factors affecting long-term medication adherence is warranted to enable better targeting of interventions.

In summary, this review flags the enormous potential for future research and nursing practice development to significantly contribute to the care and outcomes of cardiac patients through optimizing the benefits offered by medication schedules. Review findings indicate promising outcomes, but also highlight the current lack of high-quality research and knowledge deficits in this field.

2.10 Chapter Summary

This chapter presented the findings of a systematic review of studies that have examined the effectiveness of interventions that are amenable to delivery by nurses in improving the adherence of patients with CVD to their prescribed cardio-protective medications. The review demonstrated that various interventions have been reported to improve adherence to cardiovascular medications using educational or behavioural strategies, or a combination of both. Multi-component interventions tailored to address patients' health beliefs and behaviours were shown to be effective in improving adherence, including counselling strategies such as motivational interviewing (MI) and adjuvant techniques such as text message (TM) reminders.

Evidence of the effectiveness of nurse-led interventions was limited because of compromise to the quality of the research and uncertainty of which intervention components were more effective. The evidence was limited by weak methodological approaches, lack of adherence definition, varied intervention methods (multiple approaches versus single approach), and siting in various chronic care settings. Nurse-led interventions involving multiple components can be effective in enhancing adherence behaviours. The following chapter provides the results of the survey study conducted in Australia.

CHAPTER 3 Medication Adherence and Predictive Factors in Patients Attending Hospital with Cardiovascular Disease in Australia: A Cross-Sectional Survey

3.1 Introduction of the Chapter

This chapter of the thesis is based on a paper revised and submitted to Nursing and Health Science. This chapter addresses the objective, ‘to identify factors predictive of medication adherence in patients with cardiovascular disease admitted or attending hospital in Australia’. The data collected and reported in this chapter also provide information to support motivational interviewing by identifying topics predictive of medication adherence in patients with CVD in Australia. The chapter also includes description and comparison of findings from patients recruited on a cardiac ward versus patients undergoing cardiac rehabilitation, as a proxy for two different time points in the CVD journey: following an acute event and during stable self-management.

3.2 Introduction

Cardiovascular disease (CVD) is a major cause of mortality and disability worldwide (Wirtz et al. 2016). It was the main cause of mortality in 2016 in Australia, accounting for 19,077 deaths (62.4 per 100,000 population) (Australian Bureau of Statistics 2016). Adherence to cardio-protective medications is critical for primary and secondary prevention of CVD (National Heart Foundation of Australia 2011), but it is estimated that up to 50% of medications are not taken as prescribed by patients with chronic disease, increasing rehospitalization rates and premature mortality (Gandapur, Kianoush, Kelli, Misra, Urrea, Blaha, Graham, Marvel, & Martin, 2016).

The World Health Organization defines adherence to medications as "taking more than eighty percent of medicines as prescribed" (Sabaté 2003). Medication adherence typically decreases over time; this is a major challenge in all chronic diseases (Usherwood 2017). For instance, a Canadian study found that only thirty-six percent of elderly patients with CVD adhered to their cholesterol-related treatments two years after diagnosis (Jackevicius et al. 2002). An American study found that 10% -25% of patients newly diagnosed with cardiac disease had stopped taking their medications by their 24 week follow-up (Sokol et al. 2005). In Australia, cardiovascular medication non-adherence rates ranged between 14% and 43% from 2010 to 2014 (Simoni et al. 2011, McKenzie et al. 2015). Despite the increasing potential for cardiac medications to impact patients' health, the level of medication adherence in patients with CVD remains problematic (Leslie et al. 2018). For example, a recent RCT conducted in Australia showed medication adherence among patients with CVD ranging from only 18.8% to 29.4% for intervention and control groups, respectively (Santo et al. 2019). Poor adherence to medication regimes in patients with CVD is associated with frequent rehospitalization and mortality (McKenzie et al. 2015). Given that medication adherence is an important health behaviour world-wide, at all points in the treatment of CVD, it is essential to determine adherence to cardio-protective medications and potential predictive factors to initiate behavioural changes as needed.

3.3 Literature Review

Adherence to medication prescriptions is necessary to receive the full benefits of medications (Pandey et al. 2018), but is a complex and dynamic process. This is particularly challenging for patients with CVD who are predominantly discharged from hospital with long-term polypharmacy (World Health Organisation 2003). Multiple factors may be influential, including patient-related behaviors that are difficult to objectively measure and monitor (Tokdemir & Kav 2017). Patient knowledge or understanding of a medication regime, perceived adherence barriers or facilitators, low self-efficacy, and lack of belief in the necessity of medicines may influence medication adherence (Broekmans et al. 2010, Morrison et al. 2015).

Socio-demographic factors are relevant. Studies of age have returned inconsistent results: while some found those over 65 years particularly non-adherent, possibly because of cognitive impairment, physical disability and lack of social support (Pamboukian et al. 2008), others found older patients more likely to be adherent than younger patients (Park et al. 2015). Gender may affect medication adherence (Sakthong et al. 2009), but again findings are contradictory, perhaps because of the potential for error in self reporting, which may produce spurious results (Berg et al. 2004). Low medication adherence has been found to occur in more male than female patients with CVD (Manteuffel et al. 2014), and patients with heart failure (Viana et al. 2014). By contrast, female patients with CVD were shown to be less likely to adhere to cardio-protective regimes than males (Kolandaivelu et al. 2014). On the other hand, Doll et al. (2015) found neither age nor gender were linked to medication non-adherence in patients with CVD attending cardiac rehabilitation, and patients with heart failure (Hood et al. 2018). Ethnicity has shown similarly inconsistent results but has been reported as predictive of medication adherence among patients with myocardial infarction (Zhang et al. 2012). Employment status has also been found to have an effect (Kassab et al. 2013), with higher medication non-adherence rates from unemployed people, particularly those without healthcare coverage (Lee et al. 2013).

Other influences include health literacy, where poor literacy has been linked to reduced medication adherence (Gazmararian et al. 2006). Social support has generally been linked to better medication adherence, positively affecting CVD outcomes (Wu et al. 2013). One observational study found that 59.2% of patients with CVD attending cardiac rehabilitation with support from family and staff were adherent and better able to refill cardiac medications than those with no support (Molloy et al. 2008). Mood has been shown to influence patients' self-efficacy and their beliefs about medications, also affecting medication adherence (Cha et al. 2008).

The problem of medication non-adherence has been repeatedly reported among patients with various chronic diseases, and disease stages (Park et al. 2018). Cardiac patients experience a number of stages in their disease progression and treatment, including acute events and hospital admissions, referrals and attendance at cardiac rehabilitation, and community self-management (Doucette 2017). Admission to hospital for an acute health event has been noted to be associated with changes favoring more health-oriented behaviors even in the absence of any specific health behavioral intervention (Boudreaux et al. 2007). Among patients attending cardiac rehabilitation, self-efficacy (Greer et al. 2015), social support (Molloy et al. 2008) and beliefs about the benefits of exercise (Pandey et al. 2018) have all been associated with medication adherence. Few studies consider differences in medication adherence among patients with CVD at different stages of treatment (Bonow et al. 2011), although such information could be used to develop strategies for different stages (Nilsson et al. 2000). Investigating the dynamics of medication non-adherence may identify specific factors at specific points, offering the potential to enhance medication adherence at different stages (King-Shier et al. 2017). Two such pivotal points in CVD are when an acute event leads to hospitalization, and subsequent rehabilitation. There has been no evaluation of the factors leading to medication non-adherence at either stage. Overall, poor medication adherence remains a significant challenge in the management of patients with chronic diseases, including those with CVD, with a wide, locally relevant but broadly inconsistent variety of predictive factors. The underlying conceptual framework of medication adherence and factors that affect patients' adherence to their prescribed medications warrant further exploration.

3.4 Study Aims

This study part of this thesis aimed to evaluate medication adherence and predictive factors among patients with CVD who were admitted to a cardiac ward or were attending cardiac rehabilitation in Australia.

3.5 Methods

3.5.1 Design

This quantitative study used cross-sectional survey design to examine self-reported medication adherence in patients with CVD who had been admitted to hospital or were attending cardiac rehabilitation, to consider the factors associated with medication adherence. These factors include beliefs about medication, medication adherence self-efficacy, social support and the ability to refill medication. Two stages in the disease trajectory, the acute phase and rehabilitation, were chosen to determine if patterns of stage-specific predictive factors could be identified, which might lead to development of targeted nurse-led interventions to improve medication adherence at each stage.

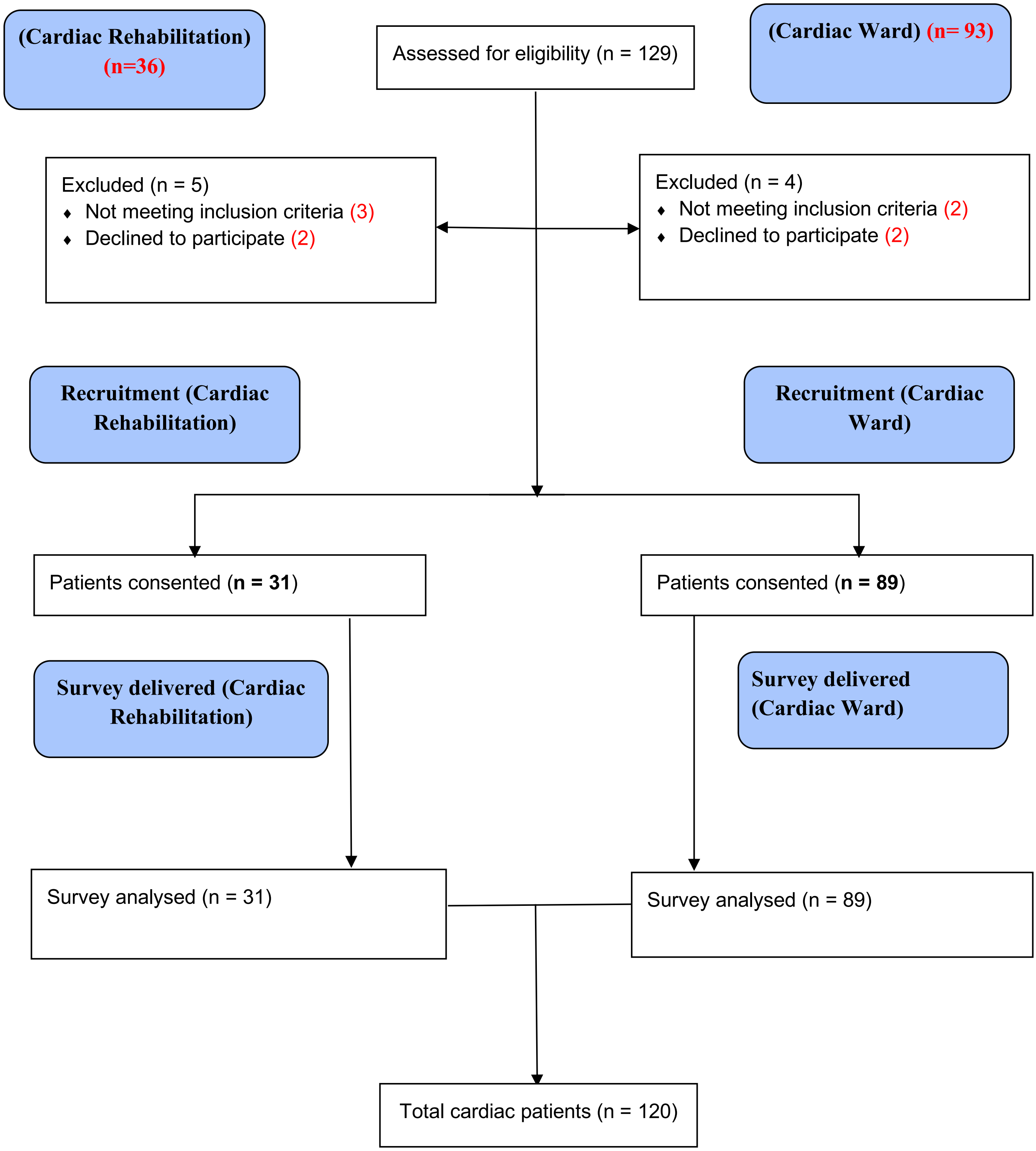
3.5.2 Participants, Sampling and Sample Size

Convenience sampling was used, based on the availability of patients and the researcher. Participants were patients with cardiac disease who were admitted to a hospital in Sydney for an acute cardiac event such as myocardial infarction or percutaneous coronary intervention or had been referred to and attended a cardiac rehabilitation program. The inclusion criteria specified adults aged 18 years and above with a diagnosis of CVD, currently treated with one or more cardiac medicines and personally responsible for taking them, who were prescribed medications prior to hospital admission or when attending cardiac rehabilitation. Participants needed to understand written and spoken English to complete the survey. Patients with vision and hearing impairment, cognitively impaired patients, those with history of psychiatric diseases, and patients who were not taking any cardiac medication were excluded (Figure 1).

3.5.3 Sample Size Determination

The sample size was designed to address the aim of identification of factors predictive of medication adherence, given a moderate sized effect. A sample size of 85 participants was calculated to demonstrate a moderate sized effect ($\alpha = 0.05$, 5% level of significance) and power = 0.80 based on medication adherence as reported by Ma et al. (2014). Taking into account contingencies such as non-response rate and recording error, the sample was further increased by 29% (n =115 participants). A total of 120 participants were recruited. The sample size was calculated based on a formula by (Viechtbauer et al. 2015). About 125 patients with CVD per month were admitted to the hospital's cardiac ward, with 18% uptake of referrals to the cardiac rehabilitation centre (unpublished hospital data). We anticipated approximately 50% of eligible patients with CVD might participate.

Figure 3.1 Flow Diagram of the Recruitment Process



3.5.4 Study Settings

The study was located in the out-patient cardiac rehabilitation centre and in-patient cardiology ward of a major acute tertiary referral hospital in Sydney, a teaching hospital of approximately 400 beds. It has in-patient diagnostic and interventional cardiac services including a cardiothoracic intensive care and sub-acute surgical ward, and a coronary care and sub-acute cardiology ward. The cardiac rehabilitation service screened patients referred from the in-patient wards and out-patient clinics and allocated them to various relevant programs, including structured group supervised exercise, information sessions, and referral to relevant services such as clinical counselling.

3.5.5 Routine Medication Care

The Australian Cardiac Rehabilitation Association recommends that routine care for cardiac patients should include: education on the importance of adherence to cardiovascular medicines including the reasons for their use, barriers to medication adherence, medication doses and frequency, and monitoring medication adherence using a tested tool (Woodruffe et al. 2014). Nurses and pharmacists are mainly responsible for providing medication education to patients with CVD during their stay in the cardiac ward and as a part of their cardiac rehabilitation. Nurses are also responsible for coordinating care with other healthcare professionals (Fridlund 2002), accordance with the standards of practice for Registered Nurses in Australia (Nursing and Midwifery Board of Australia 2016).

3.5.6 Ethical Consideration

Recruitment occurred under the supervision of the clinical nurse consultant for cardiac rehabilitation and the clinical pharmacist for the cardiac ward, with the agreement of the director of nursing and the cardiology consultant. Patients admitted to the cardiac ward and those referred to and attending the cardiac rehabilitation program were screened using the study inclusion/exclusion criteria by the clinical nurse consultant and the clinical pharmacist. Eligible members of consecutive cohorts of patients who expressed interest in the project were referred to the researcher. Approvals to conduct this study were granted by the appropriate District and university Human Research Ethics Committees in June 2016 (reference numbers: ETH16–0635 (**Appendix C**); 16/085; 16/085–HREC/16/POWH/218 (**Appendix D**) The researcher obtained written informed consent from participants for participation in the study (**Appendix E**).

3.5.7 Data Collection Procedures

A total of 129 questionnaires were distributed; 120 were returned from eligible participants with a response rate of 95%. In total 120 questionnaires were completed and formed the basis for the present analysis. On average approximately 13 participants per month were recruited from both settings. Between October 2016 and December 2017, 120 patients with CVD were recruited: 89 in-patients and 31 out-patients (Figure 3.1). Data collection took place: in the cardiac ward for in-patients, where the questions referred to medication adherence in the period immediately prior to hospital admission, and during attendance at cardiac rehabilitation in the waiting room. The questionnaires were paper-based, and data collection was by self-report. At enrolment, participants received a folder containing the study overview, the questionnaires and a consent form; the researcher also explained the purpose and methods of the study face-to-face. Recruitment procedures precluded recruitment of patients for more than one arm of the study- the cardiac rehabilitation interviews were conducted ahead of the in-patient interviews.

3.5.8 Study Instruments

The survey comprised questionnaires about patients' adherence to cardiac medication, their beliefs, behavioral and psychological factors linked with medication non-adherence in previous studies (Morisky et al. 1986, Horne et al. 1999), identified as potentially predictive of medication adherence and offering opportunities for nurse-led interventions to enhance adherence. The survey was piloted with five participants; no problems were identified. Completion took 10-15 minutes. The language was deemed manageable for those with poor literacy skills.

3.5.8.1 Socio-demographic and Health-Related Factors

Data collected in this section included: age (years), gender (male, female), employment status (employed, unemployed, retired), living arrangement (lives alone or with spouse/partner/others), marital status (married/co-habiting or not in a relationship). It also asked for years of full-time education, ethnic background (Australian/New Zealander, others), presence of co-morbidities such as hypertension, diabetes mellitus, respiratory or renal disease, and number of cardiac medications taken daily. Co-morbidities were included because increasing numbers of diseases are linked to increasing numbers of medications and both have been linked to medication adherence. Diabetes was identified separately because of the high occurrence and high burden of medication management of this disease (Nazir et al. 2016) in people with CVD (Halter et al. 2014) (**Appendix F**).

3.5.8.2 Questionnaires Addressing Medication Adherence

The validity and reliability of the study instruments to detect medication non-adherent behaviors in patients with CVD in various cardiac settings have been well established (Al-Ganmi et al. 2018). The Medication Adherence Questionnaire (MAQ) (Morisky et al. 1986) is a four-item scale used to assess medication adherence and adherence determinants such as forgetfulness, carelessness, efficacy and adverse effects. MAQ contains four simple dichotomous questions (yes/no), scoring one point for each "yes" response and zero point for each "no" response. Scores are summed to derive a total score with higher numbers demonstrating greater medication non-adherence i.e. 0 = high to 3–4 = low medication adherence behaviours. The MAQ questionnaire has been validated in various patient populations and patients with cardiac conditions such as heart failure, CVD and dyslipidaemia (Afonso et al. 2006, Nguyen et al. 2014). It has demonstrated acceptable internal consistency of α = 0.61, sensitivity 0.81 and specificity 0.44 in patients with hypertension (Lavsa et al. 2011). The MAQ score was found to be a significant independent predictor of cardiovascular medication nonadherence in a multivariate logistic regression model (Shalansky et al. 2004) (**Appendix F**).

The Adherence to Refills and Medications Scale (ARMS) (Kripalani et al. 2009) is a 12-item scale used to assess patients' ability to self-administer and refill their medications. The ARMS subscales are highly correlated with the MAQ-4 items questionnaire, and with medication refill adherence (Kripalani et al. 2009). The ARMS has been validated in patients with CVD and multiple chronic conditions (Kripalani et al. 2008) and has demonstrated high internal consistency using Cronbach's α= 0.814 (Kripalani et al. 2009) (**Appendix F**).

The Belief about Medicine Questionnaire (BaMQ) (Horne et al. 1999) consists of eight questions used to evaluate patients' beliefs about the necessity of medications plus concerns, medication overuse and general harm. The BaMQ has been shown to be a valid and reliable tool, correlated significantly with other medication adherence questionnaires such as MAQ and the Medication Adherence Rating Scale (MARS-5) (Horne et al. 1999, Mårdby et al. 2007, Gatti et al. 2009). Each BaMQ subscale has been evaluated for internal consistency using Cronbach's α (specific-necessity=0.77, specific-concerns= 0.76, general-overuse= 0.60, general-harm= 0.78) (Horne et al. 1999). The four BaMQ categories have been shown to correlate highly with patients' beliefs about the adverse effects of medication and specific-concerns as assessed by the Sensitive-Soma Scale administered to general medical and cardiac groups to demonstrate the criterion validity of BaMQ (Horne et al. 1999) (**Appendix F**).

The Medication Adherence Self-Efficacy Scale-Revised (MASES-R) (Fernandez et al. 2008) is a 13-item questionnaire to evaluate patients' confidence in taking their medications as part of everyday routine. The MASES-R has been shown to correlate significantly with electronic medication adherence records (MEMS) at three-months, confirming its predictive validity (Fernandez et al. 2008). The concurrent validity of the MASES-R has also been confirmed (Fernandez et al. 2008) (**Appendix F**).

The Medication Specific Social Support (MSSS) scale (Lehavot et al. 2011) is an eight-item scale to evaluate how often patients receive support with their medication from family, friends, or healthcare providers (Lehavot et al. 2011). The MSSS has demonstrated high internal consistency using Cronbach's α= 0.85 (Lehavot et al. 2011) (**Appendix F**). Permission to use these questionnaires was obtained from their authors

3.6 Data Analysis

Nine of the 129 questionnaires were incomplete and were not included in the analysis (**Figure 3.1**). The information regarding medication adherence was missing for these nine questionnaires. A total of 120 patients were consented and surveyed (Figure 3.1). These 120 questionnaires were fully completed, and data were analysed using IBM SPSS version 23. Descriptive statistics were conducted to analyse patients' socio-demographic characteristics, medication adherence values, medication adherence self-efficacy, beliefs about medication and social support. Among sociodemographic, health and medication-related data, continuous variables were presented as means and standard deviations, and categorical variables by frequencies and percentages (Table 1). Independent samples t-tests were used to analyse differences between patients with CVD from the cardiac rehabilitation and cardiac ward groups with continuous variables, and Chi-square ($\chi2$) tests analysed the differences with categorical variables. Medication adherence was categorized as high, medium/ low and Chi-square ($\chi2$) was used to compare the patient groups. Bivariate analyses were used to examine the association between potential medication adherence factors and medication adherence (MAQ scale) using Spearman's rank correlation coefficient (Rho). Variables significantly associated with medication adherence in these analyses were examined using logistic regression, reporting the odds ratios and confidence intervals for predictive variables with a level of significance at less than 0.25 for entry into regression models and less than 0.05 for the logistic regression test (Polit. 1996). The forced entry method was used, in which all potential predictors were forced into the model in the first step then sequentially removed. Two-sided tests were conducted with significance set at 0.05.

3.7 Results

3.7.1 Characteristics of Participants

Recruitment progressed at approximately 13 participants per month from both settings. Between October 2016 and December 2017, 120 patients with CVD were recruited as: a) in-patients of the cardiac ward (n = 89) or b) out-patients attending for cardiac rehabilitation (n = 31) (**Figure 3.1**). Most socio-demographic and health data did not differ significantly between participants in the two study settings (**Table 3.1**). Compared to participants from the cardiac ward, cardiac rehabilitation participants took significantly fewer cardiac medications per day. They tended to be better educated, more often employed, and younger, although these differences between the groups were not statistically significant (**Table 3.1**).

3.7.2 Medication Adherence

Based on the 4-item MAQ scores, 62.5% of patients in both groups were classified as high (scoring 0) and 37.5% medium/low adherent (scores 1-4) (**Table 3.2**). Since only one patient reported low medication adherence, we dichotomized the dependent variable into two groups: high adherence (score 0) and medium/low adherence (score 1-4). Medium/low adherence rate was higher among participants recruited from cardiac rehabilitation rather than the cardiac ward (41.9% versus 36.0%; respectively; p=0.001). Cardiac rehabilitation participants were also more likely to forget the names of their medications than ward participants (30.8% vs. 16.1%, respectively; p= 0.04) (**Table 3.2**). Forgetfulness was the most commonly reported reason for medication non-adherence (32.3% vs. 31.5% in out-patients and in-patients, respectively). Medication-related variables (ARMS, MASES, BaMQ, MSSS) did not differ significantly between participants recruited from the two settings (**Table 3.2**).

Table 3.1 Sociodemographic and Health Characteristics of Patients Recruited from the Cardiac Rehabilitation Department and the Cardiac Ward.

Variables	**Cardiac Rehab. (n = 31) n (%)**	**Cardiac Ward n = 89 n (%)**	**Chi-Square test**	***df***	***P*-values**
Gender					
Male	19 (61.3%)	59 (66.3%)	0.25	1	0.62
Female	12 (38.7%)	30 (33.7%)			
Employment Status					
Employed	10 (32.3%)	21 (23.6%)	7.18	2	0.03*
Unemployed	6 (19.4%)	5 (5.6%)			
Retired	15 (48.4%)	63 (70.8%)			
Living Arrangement					
Lives alone	4 (12.9%)	23 (25.8%)	2.21	1	0.14
Lives with spouse/partner/others	27 (87.1%)	66 (74.2%)			
Marital Status					
Married/ co-habiting	23 (74.2%)	54 (60.7%)	1.83	1	0.18
Not in a relationship	8 (25.8%)	35 (39.3%)			
Ethnicity					
Australian/ New Zealander	18 (58.1%)	57 (64.0%)	0.35	1	0.55
Others	13 (41.9%)	32 (36.0%)			
Comorbidity					
None	26 (83.9%)	68 (76.4%)	0.76	1	0.39
Any	5 (16.1%)	21 (23.6%)			
Diabetes Mellitus					
No	21 (67.7%)	56 (62.9%)	0.23	1	0.63
Yes	10 (32.3%)	33 (37.1%)			
			t-test	***df***	**P-values**
Age; mean (SD)*/ years	66.6 (11.9%)	69.9 (11.5)	–1.38	118	0.17
Years of full-time education; mean (SD)	13.9 (3.6)	11.9 (3.5)	2.63	118	0.01**
Number of cardiac medications taken per day; mean (SD)	2.8 (1.1)	3.2 (0.9)	2.57	118	0.01**

Note: (SD) Standard Deviation, *Significant at 0.05, **Significant at 0.01.

Table 3.2 Medication Adherence Related Variables in Patients Recruited from the Cardiac Rehabilitation Department and the Cardiac Ward

Medication adherence	Total n (%) n = 120	Cardiac Rehabilitation n (%) n = 31	Cardiac Ward n (%) n = 89	Chi-Square Test	df	P-values
MAQ level						
High (0)	75 (62.5%)	18 (58.1%)	57 (64.0%)	28.033	1	0.001*
Medium/Low (1–4)	45 (37.5%)	13 (41.9%)	32 (36.0%)			
Medications recall						
Can remember all medications	83 (69.2%)	83 (69.2%)	26 (83.9%)	4.24	1	0.04**
Can't remember all medications	37 (30.8%)	37 (30.8%)	5 (16.1%)			
Medication adherence variables	**Total n (%) n = 120**	**Cardiac Rehabilitation n (%) n = 31**	**Cardiac Ward n (%) n = 89**	**t-test**	***df***	**P-values**
ARMS mean (SD)*		45.10 (3.1)	45.72 (2.9)	–1.000	118	0.32
MASES mean (SD)*		34.06 (6.6)	35.6 (5.5)	–1.282	118	0.20
BaMQ mean (SD)*		30.3 (6.1)	31.9 (4.4)	–1.474	118	0.14
MSSS mean (SD)*		10.6 (5.6)	11.5 (7.5)	–0.577	118	0.56
MAQ individual items scores§ mean (SD)*		3.5 (0.72)	3.5 (0.8)	–0.06	118	0.95
Forget to take						
Yes n (%)	38 (31.7%)	10 (32.3%)	28 (31.5%)			
No n (%)	82 (68.3%)	21 (67.7%)	61 (68.5%)			
Careless at times						
Yes n (%)	13 (10.8%)	3 (9.7%)	10 (11.2%)			
No n (%)	107 (89.2%)	28 (90.3%)	79 (88.8%)			
Sometimes stop taking when feel better						
Yes n (%)	5 (4.2%)	1 (3.2%)	4 (4.5%)			
No n (%)	115 (95.8%)	30 (96.8%)	85 (95.5%)			
Sometimes stop taking when feel worse						
Yes n (%)	9 (7.5%)	3 (9.7%)	6 (6.7%)			
No n (%)	111 (92.5%)	28 (90.3%)	83 (93.3%)			

Note: (n) number of participants, ***(df)*** degree of freedom, (**SD**) standard deviation, (**ARMS**) Ability to Refill Medication & Self-Management, (**MASES**) Medication Adherence Self-Efficacy, (**BaMQ**) Belief about Medication, (**MSSS**) Medication Social Support.
MAQ level: (0) = All answers with 'No', (1–4) = one to four answers with 'Yes'.
§ Morisky medication adherence scale, higher scores reflect non-adherence.

p< 0.001*.
p< 0.01**.

None of the twelve sociodemographic or health variables were significantly associated with medication adherence, although the ability to refill medications (ARMS), medication adherence self-efficacy (MASES-R) and beliefs about medications (BaMQ) were all significantly associated with medication adherence (MAQ), demonstrating positive moderate-strong correlations (**Table 3.3**), which explained 45%, 15% and 11% of patients' medication adherence, respectively. Patterns of the associations revealed similar findings when the analyses were conducted separately for each group. In both groups, there was a significant link between MAQ with ARMS and MASESR (for ward patients, *Rho*= 0.655, p<0.001; *Rho*= 0.355, p<0.002, respectively; for rehabilitation patients, *Rho*= 0.716, p<00.1; *Rho*= 0.498, p< 0.005, respectively). For ward-based participants, the association between MAQ and BaMQ just missed statistical significance (*Rho*= 0.200**,** p<0.06) which was demonstrated for rehabilitation participants (*Rho*= 0.696, p<0.001).

These variables were entered in the binary logistic regression model (**Table 3.4**). The results of the analysis indicated that ability to refill cardiac medications and beliefs about cardiac medications were significant predictors of cardiac medication adherence: participants with greater ability to refill cardiac medications (Odds Ratio (OR)=0.463, p=0.001) and with more positive beliefs about their medications were more likely to report better prediction for medication adherence (OR=1.142, p= 0.04). The logistic regression analysis recorded a significant Omnibus test for the model (significance < 0.001). The Pseudo R Square statistic indicated that the model, as a whole explained between 38.7% (Cox & Snell R Square =0.387) and 52.8% (Nagelkerke R Square = 0.528) of the variance in medication adherence. ARMS + BaMQ explained 39.6% of variance but ARMS alone explained 36.6% of variance in MAQ (**Table 3.4**).

Table 3.3 Association between Medication Adherence (MAQ) and Potentially Predictive Variables in Both Participants Groups

Variables	**Rho**	**P value**
Age	–.023	0.803
Gender (Male, Female)	–.132	0.803
Location of recruitment (in-patient, out-patient)	.030	0.745
Employment status (employed, unemployed, retired)	.046	0.620
Living arrangement (Lives alone, Lives with spouse/partner/others)	.121	0.188
Marital status (married/ co-habiting, not in a relationship)	–.111	0.229
Ethnicity (Australian/ New Zealander, others)	–.155	0.092
Number of full-time years of education	–.131	0.41
Comorbidity (none, any)	–.055	0.554
Diabetes Mellitus (no, yes)	–.129	0.160
Medications recall	.099	0.281
Total number of pills/day	–.079	0.660
Ability to refill medication and self-management (ARMS)	.676**	0.001*
Medication adherence self-efficacy (MASES)	.392**	0.001*
Beliefs about medication (BaMQ)	.335**	0.001*
Medication specific social support (MSSS)	–.036	0.697

**. Spearman's rank correlation rho (odds ratio)
*. Correlation is significant at the *P*-value = 0.001 level (2-tailed)

Table 3.4 Binary Logistic Regression Model Examining Predictors of Cardiac Medication Adherence

Predictors		Odds ratio B	Standard Error S.E.	Wald	df	Sig.	Odds ratio Exp.(B)	95% C.I. EXP.(B)	
								Lower	Upper
Step 1[1]	Age	.795	.621	1.638	1	.201	2.215	.655	7.485
	Location of recruitment	.150	.631	.056	1	.813	1.162	.337	4.004
	ARMS	–.771	.170	20.520	1	.001	.463	.332	.646
	MASES	.000	.060	.000	1	.998	1.000	.889	1.124
	BaMQ	.133	.065	4.178	1	.041	1.142	1.005	1.298

a. Variable(s) entered on step 1: **Age**, **ARMS**: Ability to Refill Medication & Self-Management, **MASES**: Medication Adherence Self-Efficacy, **BaMQ**: Belief about Medication.

3.8 Discussion

More than one-third of both groups had medium/low cardiac medication adherence. Participants recruited from cardiac rehabilitation reported lower medication adherence than those recruited as cardiac ward in-patients. Medication-related variables (ARMS, MASES, BaMQ, MSSS) did not differ significantly between participants recruited from the two settings.

With well over one-third of patients with CVD reporting medium/low adherence to their medications, our findings are broadly consistent with those of the World Health Organisation (2003), which highlighted medication non-adherence at 50%, with differing predictive factors in patients with chronic diseases including HIV, depression, hypertension and CVD.

Consistent patterns of poor medication adherence in different patient groups suggests there may be common underlying problems, perhaps of inadequate patient education, or at least of patients' inadequate understanding of the importance of medication adherence, whether at the initiation of therapy or latter, in the rehabilitation phase (Woodruffe et al. 2014). Perhaps this is the result of faulty beliefs, or practical or attitudinal barriers among patients attending cardiac rehabilitation programs after acute cardiac events (Verburg et al. 2019). Understanding patients' medication adherence behaviours is the first step towards enhancing their self-management and improving patients' outcomes. This study showed unacceptable medium/low adherence to cardiac medication in both groups. In those recruited from the cardiac ward, this may have contributed to their hospital admission. The poor medication adherence reported by those undertaking rehabilitation indicates risk of recurrent cardiac disease and future hospitalization.

The logistic regression results showed that the ability to refill and administer medications significantly predicted adherence to cardio-protective medications. This finding is congruent with those of Kripalani et al. (2009), who found that patients with CVD who were better able to refill their medications and self-manage had better adherence to their medication regime. Other studies suggest that patients' ability to refill medications may be predicted by poor physical activity (Baggarly et al. 2014), younger age (Magnabosco et al. 2015), the number of daily medications, and patients' perceptions about the complexity of their medicines and ability to self-manage (Bailey et al. 1996). The ability to refill medications in a timely manner can predict medication adherence if patients have lower physical activity and mobility, or if younger patients lack understanding of their susceptibility to CVD-related complications (Magnabosco et al. 2015). Gazmararian et al. (2006) indicate that individuals with multiple medications manage refills better, as they are more focused on management of their health and resources for managing complex polypharmacy are readily available. These and other findings while sometimes inconsistent and even contradictory, make it clear that, while patients' ability to refill medications predicts medication adherence, other factors also exert significant predictive power in various groups. These findings flag the importance of examining individual patients and looking for factors, such as ability to refill medications, that may predict their medication adherence.

Like some studies, our study found that, among patients with CVD, more positive beliefs about cardiac medications were predictive of adherence to their medications. Several studies have found that patients' beliefs about the necessity of their medication were significantly predictive of medication adherence, for example in patients with hypertension (Ross & Deverell 2004), with HIV (Gonzalez et al. 2007) and with CVD (Horne et al. 2013).

Uncertainty about the necessity of taking medications predicts lower medication adherence, specifically when patients have concerns about side-effects (Mann et al. 2009). Patients who hold less than strong beliefs about their medications and have concerns about side-effects were more likely to forget or deliberately skip prescribed doses (World Health Organisation 2003). Our findings from both settings, that positive beliefs about cardiac medications predicted medication adherence, are in line with other findings and highlight an important opportunity for improvement.

According to Bandura (2004), the central determinant affecting an individual's specific behaviours is self-efficacy, which influences motivation and affects other determinants. Bivariate analyses revealed that medication self-efficacy was significantly associated with medication adherence, a finding consistent with the results of two cross-sectional studies of patients attending cardiac rehabilitation and senior centres, where self-efficacy scores were positively associated with medication adherence (Ben-Natan & Noselozich 2011, Greer et al. 2015). However, differing from the results of Morrison et al. (2015), the impact of medication self-efficacy as an independent predictor of medication adherence disappeared in our regression analysis. Perhaps this reflects characteristics of patients in the different settings of the studies and may indicate opportunities for cardiac ward and rehabilitation nurses and pharmacists to more closely examine the differences and develop different strategies to promote medication self-efficacy as a way to enhance medication adherence.

This study, like that of Wu et al. (2013), did not find sociodemographic factors as significantly predictive of medication adherence. However, other studies have found age, for example, to be a significantly predictor, and a better medication adherence to hypertension medications has been noted among older people (Pamboukian et al. 2008). Given that the patients with CVD recruited for our study from cardiac rehabilitation were young, and likely to be employed and married, we might surmise that these patients were busy and had little time for self-care, with other activities taking precedence over regular adherence to medications (Lin et al. 2012). However, our study did not show a clear effect of age; other studies, too, have been inconsistent about the ability of sociodemographic factors to predict medication adherence (Crawshaw et al. 2016).

Medication adherence, not just prescription, should be recognized as an essential focus for cardiac patients, and policy-makers should make this a priority. Medication adherence education and counselling should be prioritized for cardiac patients in all hospital settings, with education sessions and face-to-face counselling integrated into care plans. Such education and counselling may provide cardiac patients with useful knowledge and strategies to manage their medication adherence behaviours. The reinforcement of medication importance during cardiac rehabilitation and in routine follow-up visits will also improve medication refill compliance and enhance cardiac patients' beliefs in the necessity of taking their medications. Establishing medication adherence plans for patients in cardiac care settings will help nurses identify those who are likely to be non-adherent, and to target individual patients who need extra help with medication adherence.

More attention is required to the role of cardiac nurses in assessing cardiac patients' self-management and ability to refill medication, and in promoting innovative forms of follow-up that enhance their role in cardiac rehabilitation. An effective care provider-patient relationship will be an important component in building an encouraging environment to achieve treatment plan goals (Brown & Bussell 2011). Tailoring educational interventions to target cardiac patients' beliefs about cardiac medication may be an effective approach to enhance patients' beliefs about the efficacy of these medications and to increase adherence to them. Simple interventions such as: electronic prompts, interactive packages of education, reminders through text messages or phone calls using smartphone and tablet devices, all easily manageable by nurses, have been found useful in improving adherence to medication in patients with CVD (Ferdinand et al. 2017).

3.9 Study Limitations

The study was conducted in busy clinical cardiac settings where the cardiac patients were asked to complete questionnaires shortly after a rehabilitation session or (in the ward) when they were deemed clinically stable. Tiredness may have affected their attention to the survey questions, and the reported medication non-adherence rates may not have been completely accurate. Cardiac rehabilitation was a particularly challenging location for recruitment, with staff and cardiac patients time-pressured and preoccupied.

Differing sample sizes between the group of cardiac rehabilitation and cardiac ward attenders might have affected the comparative analysis, with the risk of type 1 error. A convenience sampling was used, and it was not possible to achieve equivalent samples from the two locations. Differences between site sample sizes may have limited our ability to determine significant between site differences. In spite of an overall adequate sample size, careful consideration must be paid when comparing the results for the different cardiac patient groups. In addition, data were collected from one tertiary referral hospital in Sydney, Australia. Sampling from multiple sites may have improved the representativeness of the sample. Future studies could take into account the impact of clustering and sampling.

Use of self-report questionnaires may have biased the study findings, with more socially acceptable but inaccurate responses entered, as is the case in many studies. Use of standardized surveys meant participants could only provide ranked responses to the questions, and a qualitative enquiry providing a deeper understanding of cardiac patients' perspectives would be valuable. This study did not specify a timeframe for recall of medication adherence questions. Participants may not have interpreted the instructions consistently, which may have led to inaccurate responses. Also, the predictive model assumed that the predictors occurred prior to or at the same time as the outcome variable, but this study did not specifically establish this. No data were collected on the length of CVD diagnosis among patients in the two groups, a factor that may affect adherence to medication. It is possible that intra-group variability in these parameters may have affected attitudinal and hence adherence outcomes. Further investigations are needed to confirm the predictive power of the model and to explore causation paths to medication adherence. Further studies are required to consider the internal and external validity of the predictive model and report on the measurement of predictive performance. Finally, as with many medication adherence studies, lack of a gold standard assessment introduces an element of uncertainty into the reported medication adherence assessments (Kim et al. 2011).

3.10 Conclusion

There is a need to enhance adherence to medication in patients with CVD through consideration of factors significantly associated with and predictive of medication adherence. This cross-sectional study demonstrates that ability to refill medications and positive beliefs about medication are independently predictive of greater cardiac medication adherence in patients with CVD. This suggests, first, that strategies are urgently required to improve the poor medication adherence demonstrated in this and other studies. Second, these strategies should be tailored to the factors that deter timely medication refill and are linked to more negative beliefs about medication adherence. Such interventions could include innovative educational interventions and counselling sessions by clinical nurses. Cardiac nurses have an opportunity to enhance their roles in assessing and improving cardiac patients' ability to refill medication and their beliefs about those medications which, in turn, should improve medication adherence and outcomes.

3.11 Chapter Summary

This chapter presented a quantitative result of the level of medication adherence and the factors predictive of medication adherence in patients with CVD at two sentinel points a) in-patients cardiac ward for an acute event and during early recovery and b) out-patients cardiac rehabilitation program in Australia. Findings identified the need and the opportunity to improve medication adherence for patient with CVD at both these time points in their disease journey. Participants recruited from cardiac rehabilitation reported lower levels of cardiac medications adherence than patients recruited as cardiac ward in-patients. This paper also showed that the ability to refill cardiac medications and beliefs about the necessity, concern, general harm and overuse of cardiac medications were significant factors in predicting cardiac medication adherence, thus informing future interventions to support medication adherence. Clinical nurses need to build trust with their cardiac patients in order to be able to proactively address any belief-related adherence barriers arising as a result of miscommunication due to at least cultural issues. Cultural issues have not been well articulated in the medication adherence studies that included in the systematic review neither in this chapter. The following chapter examines and compares behavioural predictive factors of medication adherence at different points in the disease trajectory, and between different cultural and geographical contexts, developed and developing countries: Australia and Iraq.

CHAPTER 4 Medication Adherence and Predictive Factors in Patients with Cardiovascular Disease: A Comparison Study between Australia and Iraq

4.1 Introduction of the Chapter

This chapter of the thesis is based on the following published manuscript:

Al-Ganmi A., Al-Fayyadh S., Abd Ali M.B, Alotaibi A., Gholizadeh L., Perry L. (2019). Medication adherence and predictive factors in patients with cardiovascular disease: A comparison study between Australia and Iraq. *Collegian.* 2019, 26, 3, 355–365 DOI:

This chapter sought to evaluate and compare adherence to cardiac medications and factors potentially predictive of medication non-adherence in patients with CVD in Australia and Iraq. This paper was published in Collegian (**Appendix L**). This journal was chosen because it seeks to promote the development and exchange of knowledge that is directly relevant to all ranges of nursing practice, and because of the journal's wide range of readership and impact factor of 1.153.

4.2 Introduction

Cardiovascular disease (CVD) is the major cause of death in both developed and developing countries (Wirtz et al. 2016). CVD encompasses a variety of disease entities and specific symptom complexes, treated by a variety of approaches, pharmaceutical, surgical and interventional radiology. In developed countries, the annual mortality associated with CVD in 2013 was 4 million people, with more than 1.4 million dying prematurely before the age of 75 years (Townsend et al. 2016). In Australia, CVD accounts for 18% of the total burden of disease and was responsible for 43,963 deaths in 2016 and more than 490,000 hospital admissions in 2014–2015 (Heart Foundation 2016). According to the Australian Pharmaceutical Benefits Scheme (PBS), the total cost of CVD medications in 2015–2016 was AU$1.448 billion for a total estimated population of

23.781.200 people (Australian Bureau of Statistics 2015), comprising 20% of the total health expenditure (Australian Institute of Health and Welfare 2017).

Prevalence rates of CVD are increasing, and particularly in Middle Eastern countries such as Iraq, where CVD accounted for 27,500 deaths in 2012, 16.5% of all-cause mortality (World Health Organization 2013). The Iraqi government subsidises the cost of a wide range of prescription medicines, including those for CVD. Government health expenditure was US$82.2 billion in 2010 with an estimated 39% spent on cardiovascular medications, totalling around US$32 billion for a population of 30.868.156 people (Al Hilfi et al. 2013). The standard of treatment and care remains suboptimal in Iraq and the healthcare system is poorly effective in managing long-term disease such as CVD (Alwan 2004). The government has the responsibility to distribute pharmaceuticals without cost the patients and users of public sector. KIMADIA (the state company for importation and distribution of drugs and medical appliances) is supported by the government budget. The government pays pharmaceuticals companies through KIMADIA and public sector patients receive medications without cost for both inpatients and outpatients in most parts of Iraq (Hamza 2015). However, in the public health sector, the supply of medicine is insufficient to cover the full period of patients' treatment due to shortages or unavailability of medicines (Shabila et al. 2012). Currently, there is no system for reimbursement of money spent by the public on private prescriptions in Iraq. Thus, ensuring the availability of medications at affordable prices is a public health priority. Due to the struggles of the Iraqi health system over the past decades, in- and out-patient health services including cardiac services need re-organising and restructuring as part of the overall health system. Direct and appropriate action to improve the primary care system is needed to foster a prevention-oriented system, targeting cardiac care services and providing momentum for behaviour change in areas such as medication adherence for patients with CVD.

Long-term management of CVD is largely based on life-style modifications such as diet, physical exercises, smoking cessation and medications are usually required over sustained periods, often for life (Australian Institute of Health and Welfare 2017). Hence, adherence to medication regimes and the ability to maintain treatment as prescribed is essential to managing symptoms, delaying or preventing disease progression, premature disability and death (World Health Organisation 2003). Unless patients living with CVD are able to maintain treatments as prescribed, the resources committed by the pharmaceutical industry and healthcare providers to drug development, diagnosis and prescription are wasted.

4.3 Background

Medication adherence is defined as the extent to which patients take medications as prescribed by their healthcare providers (World Health Organisation 2003). Poor medication adherence is a key factor impeding disease control among those with CVD (World Health Organisation 2003). Despite evidence of the effectiveness of cardiac medications such as anti-platelet agents, beta-blockers, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), and aldosterone receptor antagonists (ARA) (Levy et al. 2018) to manage CVD symptoms, non-adherence rates range from 44.4% to 61% across settings and countries (Paradkar & Sinha 2017). Studies report that adherence to cardio-protective medications is sub-optimal in both resource-limited and resource-rich countries (Chowdhury et al. 2013). This is a major problem internationally; as such, there may be lessons to learn from multi-national comparisons, studying the problem in different settings and contexts.

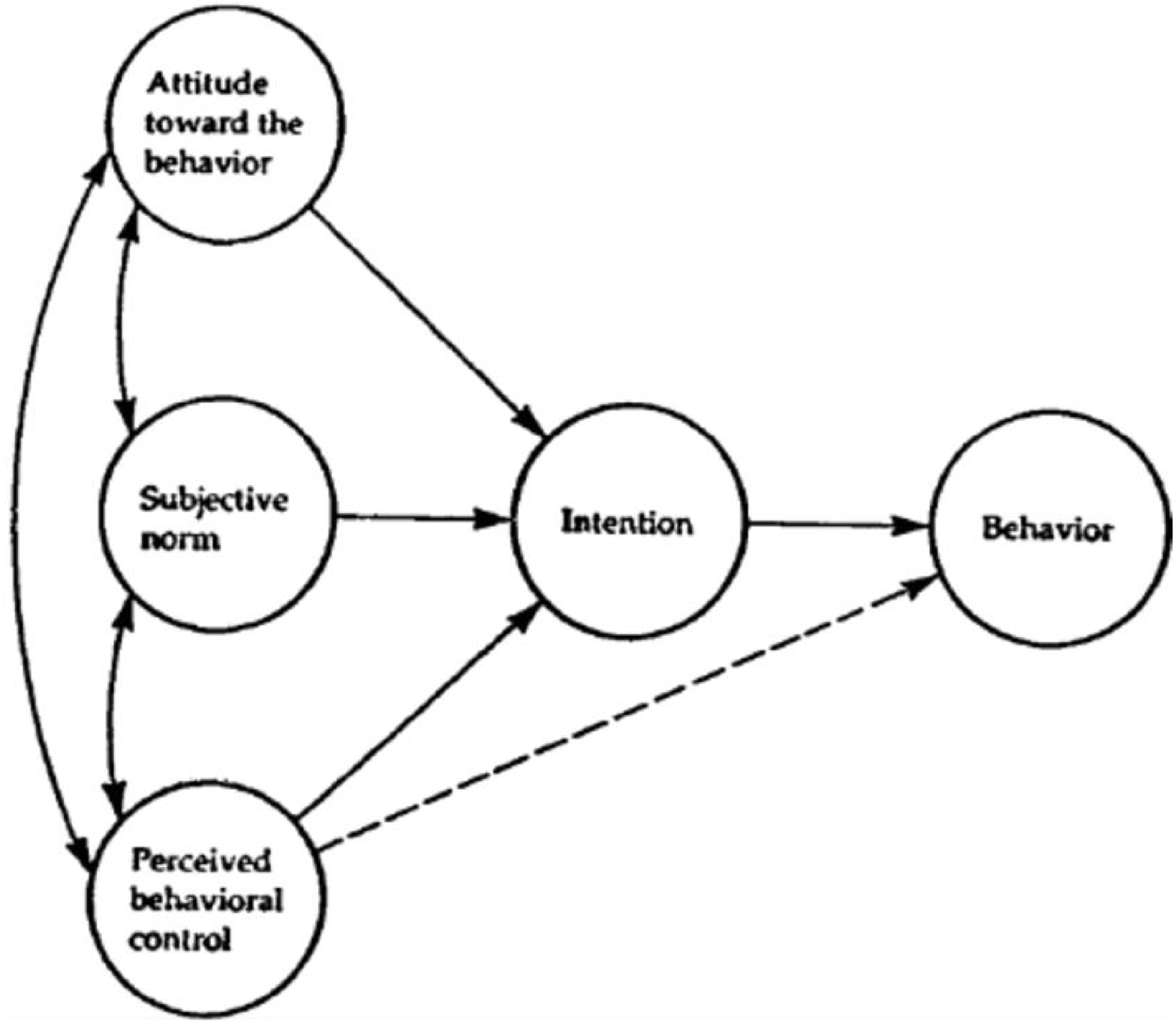
Long-term cardiac medication adherence by Australian patients with CVD is unsatisfactory, with non-adherence rates ranging between 14% and 43% from 2010 to 2014 (McKenzie et al. 2015). To date, few investigations of medication adherence have been conducted with Australian patients with chronic conditions, especially patients with CVD, and no published studies report adherence to cardiovascular medications in Iraq. Many medication adherence studies have been conducted in developed countries, but it is difficult to extrapolate the results of these studies to developing countries such as Iraq due to disparities in healthcare systems, social and cultural factors that affect health beliefs and practice (Sharrad et al. 2009). Medication non-adherence is a complex and multi-faceted problem, influenced by a wide range of sociodemographic and economic characteristics, behavioural and cognitive problems, medication complexity and social support systems (Marshall et al. 2012). Cultural differences among patients from diverse national backgrounds, racial and ethnic groups may contribute to disparities of cardiovascular medication adherence (Traylor et al. 2010). Cultural differences can negatively influence patients' beliefs about medication and their perceptions of treatment, and difference in generation, household composition and religion may also create variability in beliefs and behaviours (Horne et al. 2004). Multiple different factors may, therefore, contribute to medication non-adherence in developed and developing countries (Cooney et al. 2009).

In patients with CVD, negative perceptions of medications (Choudhry et al. 2011), beliefs about benefits and harms of medications (Horne et al. 2013), low levels of social support (Park et al. 2015), low self-efficacy (Greer et al. 2015), poor medication self-management, attitudes and sociocultural norms (Martin et al. 2005) and problems refilling medications have all been found to influence adherence to cardiac medications (Kripalani et al. 2009).

Other contributing factors include the complexity of treatment, patients' forgetfulness (Karakurt & Kaşikçi 2012), the presence of comorbidities (Al Qasem et al. 2011) and medication side effects (Molloy & O'Carroll 2017).

At an individual level, the engagement of individuals in health-related behaviours, such as medication adherence, may be explained by applying behavioural theories. This study used Ajzen (1991) Theory of Planned Behaviour (TBP) to identify factors predictive of medication adherence in patients with CVD (**Figure 4.1**). The TBP encompasses attitudes (e.g. positive or negative beliefs about the behaviour), subjective norms (e.g. the degree to which social consensus values and role models reinforce behaviours; perceived social support to perform the behaviour), and perceived behavioural control (e.g. perceptions of self-efficacy to perform the behaviour) (**Table 4.1**). The theory explains how these factors might impact patients' intentions or directly influence their behaviours such as adherence to cardiac medications (Armitage & Conner 2001). The social and cultural contexts of Australia and Iraq differ, as developed and developing nations of the West and the Middle East. However, both have high prevalence rates of CVD, and for both it is crucial to understand adherence to CVD medications and factors which predict this. Cross-national comparisons might offer information, for example cultural insights, not available with a single country study. The aim of this part of the thesis, therefore, was to explore medication adherence behaviours of patients with CVD, admitted to hospital and attending out-patient services, in Australia and Iraq and to determine factors predictive of adherence to cardiac medications regimes. Findings could inform development of preventive strategies to improve medication adherence internationally through tailored nurse-led adherence interventions utilising reliable adherence assessment tools and the most effective and appropriate adherence approaches.

Figure 4.1 Components of the Theory of Planned Behaviour Model (TPB) (Ajzen, 1991) Used to Explain Medication Adherence in this Study.



4.4 Methods

Table 4.1 Study Instruments, Adherence Characteristics Measured and their Relation to the Theory of Planned Behaviour

Instruments	Behaviours Measured	The Theory of Planned Behaviour Elements
Medication Adherence Questionnaire (4-item Morisky scale) (MAQ)	• Forgetfulness, • Carelessness, • Adverse effects • Efficacy	• Behaviour (adherence to medication)
The Adherence to Refills and Medications Scale (ARMS)	• Correct medications self-administration • Ability to refill medication on schedule	• Behaviour (ability to self-administer and refill medications)
The Belief about Medicine Questionnaire (BaMQ)	• Belief about the necessity of medications • Belief and concerns about the medication • Belief about the overuse of medication • Belief about harms of medication	• Attitudes toward the behaviour (predisposition toward adherence)
The Medication Adherence Self-Efficacy Scale-Revised (MASES-R)	• Confidence in taking medications • Ability to take medications as part of everyday routine	• Perceived behavioural control (adherence under the person's control)
Medication Specific Social Support (MSSS)	• Social support	• Subjective norms (perceived social support for adherence)

4.4.1 Aims and Objectives

The aim of this study part of the thesis was to evaluate and compare adherence to cardiac medications and factors potentially predictive of this in patients with CVD who are admitted as in-patients for acute cardiac care or those who attend cardiac rehabilitation in Australia and Iraq.

Objectives were to:

1) Identify and compare the levels of cardiac medication adherence in patients with CVD in Australia and Iraq.

2) Examine and compare socio demographic, health related, attitudinal and behavioural factors potentially predictive of medication adherence in these countries using the lens of the Theory of Planned Behaviour (TPB) (Ajzen 1991).

4.4.2 Design

This was a cross-sectional multi-centre comparative study conducted in Australia (one hospital in Sydney) and Iraq (three cardiac hospitals in Baghdad). Survey design was used to explore cardiac patients' medication adherence.

4.4.3 Study Settings

In Australia, participants were recruited from the in-patient cardiology ward and out-patient cardiac rehabilitation centre of an acute tertiary hospital in Sydney. This hospital has inpatient diagnostic and interventional cardiac services including a cardiothoracic intensive care and sub-acute surgical ward, a coronary care unit and sub-acute cardiology ward. The out-patient cardiac rehabilitation service screened in-patients and external referrals for delivery of cardiac rehabilitation programs including structured, supervised group exercise and information sessions, and referral to relevant services.

In Iraq patients were recruited at three cardiac hospitals in Baghdad, Iraq. These were major tertiary teaching hospitals offering a range of cardiac services including cardiac out-patient clinics and in-patient cardiac services for approximately 570 beds with intensive and coronary care units, cardiology and cardiac surgery departments. These three public hospitals are operated by the Iraqi Ministry of Health, which provides cardiac services for people referred nation-wide, including cardiac emergency and critical care cases. At the time of this study, most Iraqi hospitals were struggling to recover from years of war, shortages in health facilities and the health workforce, with inadequately trained healthcare professionals and poor health-care finance (The Iraqi Ministry of Health 2012).

4.4.4 Participants, Sampling and Sample Size

Participants were patients who had been admitted to hospital for an acute cardiac event or referred to and attended a cardiac rehabilitation program or out-patient cardiac clinic between October 2016 and December 2017. Similar inclusion criteria were applied in both countries: 18 years of age or older; diagnosed with cardiac disease; currently taking at least one cardio-protective medication and having primary responsibility for taking their own medication before admission to hospital or when attending cardiac rehabilitation. Participants were required to be able to read, speak and understand English (in Australia) or Arabic (in Iraq). Patients who were blind, deaf or medically deemed unable to provide consent were excluded. Patients in the cardiac ward were excluded if they were newly diagnosed with no previous history of cardiovascular disease and hence no prior history of taking prescribed cardiac medication.

Recruitment occurred under the supervision of the clinical nurse consultant for cardiac rehabilitation and the clinical pharmacist for the cardiac ward in Australia and the clinical nurse specialist for all sites in Iraq, with the agreement of the directors of nursing and the cardiology consultants of both sites. Patients were screened using the study inclusion/exclusion criteria by the clinical nurse consultant/specialist and the clinical pharmacist. Eligible members of consecutive cohorts of patients who expressed interest in the project were referred to the researcher. In Australia, approvals to conduct this study were granted by the appropriate health district (**Appendix D)** and university Human Research Ethics Committees (**Appendix C**) in June 2016 (references: 16/085 (16/085 –

HREC/16/POWH/218; ETH16–0635), and the health district Human Research Ethics Committees from the three hospitals in Iraq approved the study in June 2017 (**Appendix G**). Participants' privacy and confidentiality was maintained at all times and informed consent (**Appendix E**) obtained from all participants.

4.4.5 Sample Size Determination

A sample size of 120 participants in each country was calculated to demonstrate a moderate sized effect ($\alpha = 0.05$, 5% level of significant) and power = 0.80 (Ma et al. 2014). We anticipated approximately 50% of eligible patients might participate.

4.4.6 Data Collection Procedure

In order to assess medication adherence and associated factors, a valid, reliable and culturally acceptable instrument is required. Data collection procedures at both sites were performed under the same methods and conditions using the same instruments for the respective language after formal translation procedures had been performed in Iraq.

In both Australia and Iraq, data collection took place during patients' stay in the inpatient cardiac ward, during attendance at cardiac rehabilitation sessions, or when visiting an outpatient clinic. The study used a paper-based self-report questionnaire. At enrolment, participants received a survey package including an information sheet, a consent form and the study instruments. The researcher also verbally explained the purpose and methods of the study face-to-face.

4.4.7 The Survey

The survey comprised a number of validated questionnaires designed to gather data about medication adherence, patient beliefs, behavioural, attitudinal and other factors associated with adherence/non-adherence (**Appendix F**). For Iraqi participants, all questionnaires were formally translated and validated in the Arabic language using best practice translation guidelines (Sousa & Rojjanasrirat 2011) (**Appendix H**) .

Study instruments were translated into Arabic and then back-translated to English by two researchers independently (Epstein et al. 2015). The researcher used the back-translation method for achieving linguistic translations equivalent to the items in the source language (Duffy 2006). Following the instrument translation recommendations, an expert translator translated the English versions of the questionnaires into Arabic. The Arabic translated version was then back-translated to English by an independent expert with rich clinical experience in cardiology nursing, bilingual and fluent in both English and Arabic languages but unfamiliar with the study. The researcher then discussed and resolved minor rewording conflicts. All translations were conducted using clear, direct and simple phrases and questions suitable for older adults with low literacy levels. Content and face validity of the study questionnaires were assessed and confirmed by seven content experts with extensive experience in cardiac disease of various specialty backgrounds (cardiologist, senior pharmacists, cardiac nurse specialist and nursing educators). They reviewed the questionnaires using the Content Validity index, resulting in the wording of some items being slightly revised. The translated questionnaires were piloted with five cardiac patients from the three Iraqi hospitals; further minor modifications were made so the questionnaires could be easily understood. Sociodemographic and health data were collected, and completion took 10–15 minutes (**Table 4.2**).

Table 4.2 Sociodemographic and Health Characteristics of Cardiac Patients Recruited in Australia and Iraq.

Variables	Total (N = 246)	Australian Patients (N = 120)	Iraqi patients (N = 126)	Chi^2 test	*df*	*P*-values
Gender n (%)						
Male	161 (65.4)	78 (65.0)	83 (65.9)	0.21	1	0.89
Female	85 (34.6)	42 (35.0)	43 (34.1)			
Patient services n (%)						
Cardiac Rehabilitation/ Outpatient clinics	67 (27.2)	31 (25.8)	36 (28.6)	0.23	1	0.63
Cardiac ward	179 (72.8)	89 (74.2)	90 (71.4)			
Employment Status n (%)						
Employed	76 (30.9)	31 (25.8)	45 (35.7)	71.52	2	0.001*
Unemployed	72 (29.3)	11 (9.2)	61 (48.4)			
Retired	98 (39.8)	78 (65.0)	20 (15.9)			
Living Arrangement n (%)						
Lives alone	41 (16.7)	27 (22.5)	14 (11.1)	5.74	1	0.017*
Lives with spouse/partner/others	205 (83.3)	93 (77.5)	112 (88.9)			
Marital Status n (%)						
Married/ co-habiting	194 (78.9)	77 (64.2)	117 (92.9)	30.35	1	0.001*
Single	52 (21.1)	43 (35.8)	9 (7.1)			
Education n (%)						
<Year 11	95 (38.6)	49 (40.8)	46 (36.5)	26.49	4	0.001*
Year 12	71 (28.9)	20 (16.7)	51 (40.5)			
Certificate or Diploma	41 (16.7)	28 (23.3)	13 (10.3)			
Bachelor Degree	28 (11.4)	13 (10.8)	15 (11.9)			
Graduate Qualification	11 (4.5)	10 (8.3)	1 (0.8)			
Comorbidity n (%)						
None	168 (68.3)	94 (78.3)	74 (58.7)	10.90	1	0.001*
Any	78 (31.7)	26 (21.7)	52 (41.3)			
Diabetes Mellitus n (%)						
No	157 (63.8)	77 (64.2)	80 (63.5)	0.12	1	0.912
Yes	89 (36.2)	43 (35.8)	46 (36.5)			
Medications recall n (%)						
Recalled all medications	155 (63.0)	83 (69.2)	72 (57.1)	3.81	1	0.51
Can't recall all medications	91 (37.0)	37 (30.8)	54 (42.9)			
				t-test	***df***	**P-values**
Age, mean (SD)*/ years	69.5 (13.9)	69.1 (11.6)	54.3 (12.0)	*t* = 9.82	244	0.001**
Number of cardiac medications taken per day; mean (SD)	2.9 (1.2)	2.5 (0.98)	3.3 (1.2)	*t* = –5.71	244	0.001**

Note: (SD) Standard Deviation, *Significant at 0.05, **Significant at 0.01.

4.4.8 Medication Adherence Questionnaire

The Medication Adherence Questionnaire (MAQ) scale (Morisky et al. 1986), is a short, self-reported measure designed to assess medication adherence behaviour and barriers such as forgetfulness, carelessness, adverse effects and efficacy. MAQ contains four simple dichotomous questions (yes/no), scoring one point for each "yes" response and zero point for each "no" response. Scores are summed to derive a total score with higher numbers demonstrating greater medication non-adherence i.e. 0 = high to 3–4 = low medication adherence behaviours. The validity and reliability of the MAQ was originally established in patients with hypertension, with internal consistency of $\alpha = 0.61$, sensitivity of 0.81 and specificity of 0.44 (Lavsa et al. 2011). The MAQ score has been demonstrated to be a significant independent predictor of cardiovascular medication nonadherence by multivariate logistic regression (Shalansky et al. 2004) (**Appendix F**).

4.4.8.1 The Adherence to Refills and Medications Scale

The 12-item scale Adherence to Refills and Medications Scale (ARMS) (Kripalani et al. 2009) was used to determine medication adherence self-regulation. The ARMS consists of 12-items, the first 8 items in the scale assessing the ability to self-administration for the prescribed medications and the last four items evaluating the patient's ability to take medications on schedule. Each item is scored on a four-point scale ranging from l = none of the time to 4 = all the time. Scores are summed to derive a total score with higher numbers demonstrating better refill ability for medications on schedule. The ARMS and its subscales have been shown to correlate highly with other measures of medication adherence such as the four-item scale by Morisky and colleagues, and medication refill adherence (Mayberry et al. 2013). The ARMS has demonstrated high internal consistency among patients with low literacy skills (Kripalani et al. 2009) (**Appendix F**).

4.4.8.2 The Belief about Medicine Questionnaire

The short (eight-item) version of the Belief about Medicine Questionnaire (BaMQ) (Horne et al. 1999) was used to evaluate patients' beliefs about medications. The BaMQ identifies patients' beliefs in the necessity of and concerns about their medicines. The BaMQ is composed of subscales (8 items) to assess specific necessity, specific concerns, general overuse and general harm. Each item is measured using a 5-point Likert scale range from 1 = strongly disagree to 5 = strongly agree. Scores are summed to derive a total score with higher numbers demonstrating more positive beliefs. The internal consistency of the BMQ scale has been evaluated using Cronbach's alpha, showing inter-item correlation of General Harm = 0.44, $p < 0.01$); General Overuse = 0.64, $p < 0.01$); Specific Necessity = 0.79, $p < 0.01$); and Specific Concerns = 0.56, $p < 0.01$) (Schüz et al. 2011). The BaMQ has been shown to correlate significantly with other adherence-related scales such as the MAQ, the Morisky Medication Adherence Scale (MMAQ), and medication adherence rating scale (MARS-5) (Mårdby et al. 2007) (**Appendix F**).

4.4.8.3 The Medication Adherence Self-Efficacy Scale-Revised

The 13-item Medication Adherence Self-Efficacy Scale-Revised (MASES-R) (Fernandez et al. 2008) was used to evaluate an individual's ability to adhere to their medication schedule under various challenging circumstances. The MASES-R consists of items that specifically examine patients' confidence in taking medications in specific circumstances and their ability to take medications as part of everyday routine. Each item is measured using a 4-point Likert scale, ranging from 0 = not at all sure to 3 = extremely sure, with greater self-efficacy indicated by higher scores and a single score derived as the mean of all items. The MASES-R has been found correlate to significantly with electronic medication adherence records (MEMS) at 3 months, indicating support for the predictive validity of the MASES-R (Fernandez et al. 2008) (**Appendix F**).

4.4.8.4 Medication Specific Social Support

An eight-item Medication Specific Social Support (MSSS) scale (Lehavot et al. 2011) was used to identify how often patients receive assistance from others with their medication. Each item is measured using a 5-point Likert score for each item ranging from 0 = never to 4 = very often., with a high total mean of all items representing a high level of medication-specific support (**Appendix F**).

4.5 Data Analysis

Data were checked and cleaned prior to entry into SPSS for Windows version 23. Descriptive statistics were used to analyse data related to the patients' baseline characteristics in Australia and Iraq, level of medication adherence, medication adherence self-efficacy, beliefs about medication and social support. Optimal adherence was defined as having a score of greater than two on the four-item Morisky medication adherence scale. Bivariate analyses were conducted using the Spearman Correlation Coefficient to examine factors potentially associated with medication adherence. The levels of medication adherence were categorised as high and low/medium and compared between the two patient groups by Chi-square ($\chi 2$) test. Variables significantly associated with medication adherence in bivariate analyses were examined by logistic regression, with significance set at $P < 0.25$ in the preliminary bivariate analysis for entry into regression models and P <

0.05 for the regression analysis (Polit. 1996). Two sided tests were conducted and for all analyses, p values of <0.05 were considered statistically significant.

4.6 Results

4.6.1 Characteristics of Participants

Recruitment progressed at approximately 13 participants per month in a single general hospital in Australia and 20 participants per month at three specialised cardiac hospitals in Iraq. Between October 2016 and December 2017, in total 246 patients with CVD were recruited, n = 120 in Australia, n = 126 in Iraq, as: a) in-patients of a cardiac ward (n = 179) and b) out-patients attending cardiac rehabilitation in Australia and out-patient clinics in Iraq (n = 67).

The characteristics of participants from Australia and Iraq are presented in **Table 4.2**. Sociodemographic, health and medication-related continuous data were provided by means and standard deviations, and categorical data by frequencies and percentages. Differences between patients from Australia and Iraq were tested using independent samples t-tests for continuous variables and Chi-square ($\chi 2$) test for categorical variables. Overall, Iraqi cardiac participants were significantly younger ($t = 9.82$, $p = 0.001$) and more likely to be unemployed (chi2 = 71.52, $p = 0.017$), married or in a co-habiting relationship (chi2 = 30.35, $p = 0.001$). They were also significantly more likely to have a lower level of education (chi2 = 26.49, $p = 0.001$), comorbid disease (chi2 = 10.90, $p = 0.001$), and to take significantly more and different classes of cardiac medications per day than Australian cardiac participants ($t = –5.71$, $p = 0.001$).

4.6.2 Medication Adherence

Significantly more participants from Iraq reported medium/low levels of adherence to their cardiac medications compared to participants from Australia (64.3% versus 37.5%, respectively) and fewer reported high levels of adherence to their cardiac medications than participants recruited in Australia (35.4% versus 62.5%); both p = 0.001 (**Table 4.3**). Significant associations were sought between socio-demographic and medication-related variables and medication adherence (**Tables 4.4**). In neither country were the sociodemographic or health variables significantly associated with medication adherence.

Table 4.3 Comparison the Level of Medication Adherence in Patients with CVD in Australia and Iraq

Level of medication adherence (MAQ)	Total (n = 240)	Australian Sample (n = 120)	Iraqi Sample (n = 126)	Comparison t	df	P-value
High	120 (48.8%)	75 (62.5%)	45 (35.7%)	4.089	119	0.001*
Medium/Low	126 (51.2%)	45 (37.5%)	81 (64.3%)			

Note: (n) number of participants, ***(t)*** paired sample t-test, ***(df)*** degree of freedom.

* Significant at 0.001.

Table 4.4 Associations between Medication Adherence (MAQ) and Potential Predictors Variables in Australia and Iraq

Variables	MAQ Australia		MAQ Iraq	
	****Rho**	**P value**	****Rho**	**P value**
Age	–.023	0.803	–.016	0.810
Gender	–.132	0.803	–.223	0.114
Location of Recruitment	.030	0.745	.013	0.971
Employment	.046	0.620	–.099	0.284
Living arrangement	.121	0.188	–.178	0.51
Marital status	–.111	0.229	–.127	0.169
Number of full-time years of education	–.131	0.41	–.119	0.635
Comorbidity	–.055	0.554	–.101	0.432
Diabetes Mellitus	–.129	0.160	–.121	0.179
Medications recall	.099	0.281	–.251	0.132
Total number of pills/day	–.079	0.660	–.164	0.54
Ability to refill medication and self-management	.676**	0.001*	.588**	0.001*
Medication adherence self-efficacy	.392**	0.001*	.416**	0.001*
Beliefs about medication	.335**	0.001*	.018	0.739
Medication specific social support	–.036	0.697	–.064	0.485

** Spearman's Rho values
* Correlation significant at the *P*-value = 0.01 level (2-tailed)

The ARMS included 12-items measuring the ability to self-administer prescribed medications and evaluating the patient's ability to take medications on schedule. Mean scores for the ability to self-administer medications for the Australian participants (ranging from 23–40) and the Iraqi participants (ranging from 20–40) were 38.05 (SD = 2.69) and

33.72 (SD = 4.98), respectively (**Table 4.5**). Mean scores for the ability to refill medications on schedule (the last 4 items) for the Australian and Iraqi participants (ranging from 8 to 16) were 14.95 (SD = 1.26) and 12.64 (SD = 2.21), respectively. Mean scores for the ability to refill medication were highest in the Australian participants for the item "How often do you put off refilling your medicines because they cost too much money?" (mean = 3.94, SD = 0.23) and in Iraqi participants for the item "How often do you decide not to take your medicine?" (mean = 3.59, SD = 0.68). Lowest reported mean scores for both Australian and Iraqi participants were for the item "How often do you plan ahead and refill your medicines before they run out?" (mean = 3.43, SD = 0.9; mean = 3.25, SD = 0.75, respectively) (**Table 4.5**).

The BaMQ is composed of 8 items comprising subscales to assess specific necessity, specific concerns, general overuse and general harm. For Australian and Iraqi participants, mean scores for beliefs about the necessity of medications (ranging from 18 to 49 and 8 to 49, respectively) were 44.33 (SD = 6.14) and 34.57 (SD = 11.05), respectively. Mean scores for concerns about medication were 5.05 (SD = 2.10) and 5.66 (SD = 2.11), respectively. Mean scores about beliefs about the overuses of medication were 4.45 (SD = 1.73) and 5.62 (SD = 2.14), respectively. Mean scores about beliefs about the harms of medication were 4.13 (SD = 1.45) and 4.88 (SD = 2.24), respectively (**Table 4.5**). In this scale, most positive beliefs (highest scores) were reported for the item "My medicines protect me from becoming worse" (mean = 4.6, SD = 0.67; mean = 4.25, SD = 0.71 for Australian and Iraq participants, respectively). Lowest scores were reported for the item "People who take medicines should stop their treatment for a while every now and again" (mean =1.83, SD

= 0.91) for Australian participants, but. the item “Medicines do more harm than good” had the lowest reported scores (mean = 2.37, SD = 1.19) amongst Iraqi participants.

The medication adherence Self-Efficacy Scale-Revised consists of 13-items to assess patients’ confidence in taking medications and their ability to take medications as part of everyday routine. Mean MASES-R scores (ranging from 8 to 39) for Australian participants was 35.2 (SD = 5.78) and (ranging from 5 to 39) for the Iraqi participants was 27.1 (SD = 8.92) (**Table 4.5**). The highest score reported for the item “I feel confident to make taking my medicines part of my routine” for both Australian and Iraqi participants (mean= 2.84, SD = 0.43; mean = 2.33, SD = 0.85), respectively. For Australian participants, lowest scores were reported for the item “I feel confident taking my medicine when I worry about taking them for the rest of my life” (mean = 2.57, SD = 0.77); for Iraqi participants, the item “I feel confident taking my medicine when I feel well” (mean = 1.90, SD = 1.07) was scored lowest.

Mean scores for the Medication Specific Social Support scale (ranging from 0 to 32) for the Australian sample were 11.42 (SD = 7.02) and (ranging from 0 to 40) for the Iraqi sample was 10.57 (SD = 9.13) (**Table 4.5**). The highest scored item by the Australian group was “How often has someone in the past helped you understand information about your medicines?” (mean = 1.86, SD = 1.19), but for the item “How often has someone in the past picked up your cardiac medicines prescriptions for you?” in the Iraqi group (mean = 2.69, SD = 1.3). The lowest scored item was “How often has someone in the past called you specifically to ask how you were doing with your cardiac medicines?” for both Australian and Iraqi participants (mean = 0.87, SD = 1.24; mean = 1.61, SD = 1.69, respectively).

Table 4.5 Descriptive Statistics of Differences Between Mean Scores for Medication Adherence Scale Items of Australian and Iraqi Participants Samples

Instruments	Australia	Mean (SD)	Iraq	Mean (SD)*
The Adherence to Refill and Medication Questionnaire (ARMS)[a]	How often do you plan-ahead and refill your medicines before they run out?	3.43 (0.9)	How often do you decide not to take your medicine?	3.59 (0.68)
	Self-Administration (Behaviour) (Total score)	38.05 (2.69)	Self-Administration (Behaviour) (Total score)	33.72 (4.98)
	How often do you put off refilling your medicines because they cost too much money?	3.94 (0.23)	How often do you plan-ahead and refill your medicines before they run out?	2.58 (0.96)
	Ability to refill medications (Total score)	14.95 (1.26)	Ability to refill medications (Total score)	12.64 (2.21)
The Belief about Medicine Questionnaire (BaMQ)[b]	My medicines protect me from becoming worse	4.6 (0.67)	My medicines protect me from becoming worse	4.25 (0.71)
	Belief about the necessity of medications (Total specific-necessity score)	44.33 (6.14)	Belief about the necessity of medications (Total specific-necessity score)	34.57(11.05)
	People who take medicines should stop their treatment for a while every now and again	1.83 (0.91)	Medicines do more harm than good	2.37 (1.19)
	Belief about the overuse of medication (Total general-overuse score)	4.45 (1.73)	Belief about the general harm of medication (Total general-harm score)	4.88 (2.24)
The Medication Adherence Self-Efficacy-Revised Questionnaire (MASES-R)[c]	I feel confident to make taking my medicines part of my routine	2.84 (0.43)	I feel confident to make taking my medicines part of my routine	2.33 (0.85)
	I feel confident taking my medicine when I worry about taking them for the rest of my life	2.57 (0.77)	I feel confident taking my medicine when I feel well	1.90 (1.07)
	Medication adherence self-efficacy (Total score)	35.2 (5.78)	Medication adherence self-efficacy (Total score)	27.1 (8.92)
The Medication Specific Social Support Questionnaire (MSSS)[d]	How often someone in the past helped you understand information about your medicines?	1.86 (1.19)	How often someone in the past picked up your cardiac medicines prescriptions for you?	2.69 (1.3)
	How often someone in the past called you specifically to ask how you were doing with your cardiac medicines?	0.87 (1.24)	How often someone in the past called you specifically to ask how you were doing with your cardiac medicines?	1.61 (1.69)
	Medication specific social support (Total score)	11.42 (7.02)	Medication specific social support (Total score)	10.57 (9.13)

a: ARMS scale range is 1–4, assessed correct self-administration for medications and the patient's ability to take medications on schedule: (1) none of the time, (2) Some of the time, (3) Most of the time, and (4) All the time. **b**: BaMQ scale range is 1–5, assessed degree of agreement with each sentence: (1) Strongly Disagree, (2) Disagree, (3) Uncertain, (4) Agree, and (5) Strongly Agree. **c:** MASES scale range is 0–3, assess the degree of confident with each statement: (0) Not at all sure, (1) A little sure, (2) Fairly sure, (3) Extremely sure. **d**: MSSS scale range is 1–5, assess how often patients receive assistance from others with their medication: (1) Never, (2) Rarely, (3) Sometimes, (4) Often, (5) Very often. ***SD**: Standard Deviation

Binary logistic regression analysis was used to assess the predictors of medication adherence examining the samples from both countries together and separately. The rationale for building predictive models for the whole sample (Iraqi and Australian participants) and also separately for each country was to examine whether there were similarities in these models or consistent patterns of predictive factors. After adjusting for confounding factors, five potential predictors including age, location of recruitment (cardiac ward versus cardiac rehabilitation or outpatient clinic), ability to correctly self-administer and refill medications, medication adherence self-efficacy and beliefs about medication were included in the models. For the combined sample, country of origin was also added (**Table 4.6**) but was not found to exert significant effect. In all the models, patients' ability to correctly self-administer and refill their medications was significantly predictive of their reported adherence behaviours (**Tables 4.6, 4.7a, 4.7b**). In the Australian model (**Table 4.7a**), beliefs about medications made a small additional significant contribution (odds ratio = 1.142, 95% CI: 1.005–1.298, p = 0.041). In the Iraqi sample (**Table 5b**), beliefs about medications (odds ratio = 1.224, 95% CI: 1.090–1.375, p = 0.001) as well as location of recruitment (cardiac ward versus cardiac clinics) were also significantly predictive, with patients recruited from an out-patient cardiac clinic significantly more likely to report adherence that patients recruited in a cardiac ward (odds ratio = 0.300, 95% CI: 0.093–0.966, p = 0.044) (**Table 4.7b**).

All the models recorded significant Omnibus tests ($p < 0.001$). In the combined sample model, the Pseudo R Square statistic indicated that the model as whole explained 39.4% (Cox and Snell R Square = 0.394) and 52.5% (Nagelkerke R Square = 0.525) of the variance in cardiac medications adherence. ARMS + BaMQ explained 39.6% of variance but ARMS alone explained 36.6% of variance in MAQ. In the separate Australian and Iraqi samples, the Pseudo R Square statistic indicated that the models as whole explained between 38.7%

versus 42.6% (Cox and Snell R Square = 0.387 versus 0.426) and 52.8% versus 58.5% (Nagelkerke R Square = 0.528 versus 0.585, respectively) of the variance in cardiac medications adherence, respectively.

Table 4.6 Binary Logistic Regression Model Examining Variables Potentially Predictive of Cardiac Medication Adherence in the Combined Australian and Iraqi Participant Sample.

Predictor Variables		Odds ratio B	Standard Error S.E.	Wald	Cox and Snell R square	df	Sig.	Odds ratio Exp(B)	95% C.I. EXP(B) Lower	Upper
Step	Age	–.014	.015	.942	1	.332	.986	.957	1.015	–.014
1[a]	Country of sample	.772	.496	2.421		1	.120	2.165	.818	5.728
	Location of recruitment	.604	.371	2.646		1	.104	1.830	.884	3.789
	ARMS	.479	.078	37.538	.355	1	.001	1.615	1.385	1.883
	MASESR	.028	.030	.870		1	.351	1.029	.969	1.091
	BaMQ	–.063	.036	3.046		1	.081	.939	.874	1.008
	MSSS	–.012	.023	.283		1	.594	.988	.945	1.033
	Constant	– 20.999	3.609	33.861		1	<.000	.000		

a. Variable(s) entered on step 1: Age, Country, Location of recruitment, ARMS, MASESR, BaMQ, MSSS.

Table 4.7a Binary Logistic Regression Model Examining Factors Potentially Predictive of Cardiac Medication Adherence in an Australian Participants Sample.

Predictors	Odds ratio B	Standard Error S.E.	Wald	Cox and Snell R square	df	Sig.	Odds ratio Exp(B)	95% C.I. EXP(B) Lower	Upper
Age	.795	.621	1.638		1	.201	2.215	.655	7.485
Location of recruitment	.150	.631	.056		1	.813	1.162	.337	4.004
ARMS	–.771	.170	20.520	.396	1	.001	.463	.332	.646
MASESR	.000	.060	.000		1	.998	1.000	.889	1.124
BaMQ	.133	.065	4.178		1	.041	1.142	1.005	1.298
Constant	30.220	6.990	18.689		1	<.000	133138483 46410.104		

Table 4.7b Binary Logistic Regression Model Examining Factors Potentially Predictive of Cardiac Medication Adherence in an Iraqi Participant Sample.

	Predictors	Odds ratio B	Standard Error S.E.	Wald	Cox and Snell R square	df	Sig.	Odds ratio Exp(B)	95% C.I. EXP(B) Lower	Upper
Step 1[a]	Age	.033	.023	2.101		1	.147	1.034	.988	1.082
	Location of recruitment	–1.204	.597	4.069		1	.044	.300	.093	.966
	ARMS	–.413	.093	19.926	.426	1	.001	.661	.552	.793
	MASESR	–.067	.041	2.586		1	.108	.935	.862	1.015
	BaMQ	.202	.059	11.633		1	.001	1.224	1.090	1.375
	Constant	14.026	3.589	15.276		1	.000	1234380.440		

a. Variable(s) entered on step 1: Age, Location of recruitment, ARMS, MASESR, BaMQ.

4.7 Discussion

To our knowledge, this is the first study to report and compare adherence to cardiac medications and associated factors in patients with CVD in Australia and Iraq. Based on our findings, self-reported adherence to cardiac medications in both Australian and Iraqi patients with CVD was far from optimal. Adherence to cardiac medications was suboptimal in Australian patients, with 37.5% not achieving reasonable levels; similar problems have also been reported in cross-sectional survey of patients with chronic disease in Australia (Laba et al. 2015). In developed countries, long-term medication adherence for chronic diseases has been reported to range from 30–70% of treated patients (Degli Esposti et al. 2012). Non-adherence has been reported by 39% of Italian patients with ischaemic stroke (Colivicchi et al. 2007) and by 38.3% of Canadian patients with heart failure (George & Shalansky 2007). The results of a meta-analysis indicated unsatisfactory long-term cardiac medication adherence in Australian patients with CVD, with prevalence rates of medication non-adherence ranging between 14% and 43% in 2010 to 2014 (McKenzie et al. 2015).

Compared to developed countries, in developing countries medication adherence rates have been generally reported as lower (Ma 2016), reflected in our findings where Australian patients were significantly more likely to have high adherence compared to patients from Iraq. These findings align with other studies from other developing countries: non-adherence was reported by 41.5% of patients with hypertension in southwest Nigeria (Osamor & Owumi 2011) and 51.5% of patients with CVD in Kyrgyzstan (Murphy et al. 2016). Similarly, 54.2% of Palestinian patients with hypertension (Al-Ramahi 2015) and 58.1% of Malaysian patients with CVD (Khonsari et al. 2015) were non-adherent. Our study showed suboptimal adherence levels for a significant proportion of the cohorts in both countries, indicating the need for urgent attention. Study findings demonstrated significant differences in sociodemographic characteristics between Australian and Iraqi samples. However, none of the sociodemographic characteristics were found to be statistically associated with medication adherence. In comparing the two countries, major differences in socioeconomic development and health disparities may be reflected between the two groups as developed and developing countries. The healthcare system in Iraq, including cardiac disease management, is in early stages of development, which may relate to the low rates of adherence to cardiac medications seen in this study. The cultural implications and perceptions about taking medications may differ between developed and developing countries in terms of knowledge, attitudes and beliefs, and these may underpin medication adherence behaviours, especially for ethnic minority groups (Alzubaidi et al. 2015). Likewise, cultural differences in the understanding of chronic disease and the role of therapy, healthcare attendance, and the interactions between patients and healthcare professionals in developed and developing countries may profoundly influence the prevalence of medication adherence (Bowry et al. 2011). Further studies are required to add detail to the patterns of non-adherence in relation to specific cardiac medications in Australia and Iraq, and then to promote interventions in frontline cardiac care settings, testing their ability to enhance adherence to medications and to have significant impact on morbidity and mortality rates.

4.7.1 Factors Associated with Medication Adherence

There is currently limited knowledge of factors associated with medication non-adherence in patients with CVD, with little work exploring knowledge, attitudes, beliefs and related behaviours (Crowley et al. 2015). In both Australia and Iraq, analysed as a combined sample or individually for each country, the ability to correctly self-administer and refill medications significantly ($p<0.001$) predicted adherence behaviours. This suggests major behavioural drivers may be similar across countries despite cultural differences. These findings are consistent with the results of previous studies with other patient groups, such as Swiss patients with hypertension (Zeller et al. 2008), American patients on warfarin therapy (Orensky & Holdford 2005) and patients with CVD in Canada (Reidel et al. 2008), where the ability to refill medication independently predicted adherence behaviour but with the association declining with increasing regime complexity.

The elements of the TPB conform to and define the ability to refill cardiac medication and beliefs about medication as attitudes and behaviours that predict greater medication adherence and mediate the relationship between treatment and medication adherence. Poorer ability to self-administer and refill medications can be due to poor patient knowledge about treatments, particularly in older patients (Ratanawongsa et al. 2013); to cognitive dysfunction (Platt et al. 2008), low social support (Park et al. 2015) and lower economic status (World Health Organisation 2003). Healthcare professionals should ensure that all patients have adequate knowledge, skills and understanding in self-administration of their medications. This is particularly important in older populations, as these skills may tend to decline with age and increase with forgetfulness.

In addition, in the current study, beliefs about medication were a significant predictor of cardiac medication adherence: findings that provide further support to the Theory of Planned Behaviour. According to this theory, individuals' beliefs are strong predictors of their intentions and possibly of actual health behaviours such as medication adherence (Ajzen 1991). This study findings are in line with the TPB proposition that medication adherence intention can be influenced by patient attitudes toward adherence behaviour, which can be determined by their beliefs about the necessity of performing this behaviour (Redding et al. 2000). The behavioural intention of medication adherence might also be influenced by factors which may be beyond an individual's control, including ability to refill medications and their psychosocial and health characteristics.

These findings are congruent with those of Ruppar et al. (2012)), who found that stronger belief in the necessity of antihypertensive medications could predict better adherence among American patients (OR = 2.027, P = 0.024; CI: 1.097–3.645). Similarly, in patients with negative beliefs about the necessity of their medications, non-adherence rates were double that of those with less negative beliefs (Gatti et al. 2009). These patients were more likely to intentionally skip doses and report forgetfulness (World Health Organisation 2003). Similar findings have been reported in studies conducted in Oman, where stronger beliefs about the necessity of hypertensive medications were significant predictors of medication adherence (Al-Noumani et al. 2017).

The BaMQ coefficients in the regression equation were 0.133 for Australian (Table 4.7a) and 0.202 for Iraqi participants (Table 4.7b). However, when the combined Australian and Iraqi participant data were analysed in one logistic regression analysis, a negative coefficient (-0.063) for the BaMQ variable was found (Table 4.6). This instability may indicate that the beliefs of Australian and Iraqi cardiac patients may differ in ways that mean it is not reasonable to combine them, but more detailed data collection and further analysis would be required to unpack this.

Studies have suggested that patients' ability to self-administer and refill medications and their beliefs about medications may be affected by their level of education (Park et al. 2015), the number of prescribed medications (Karakurt & Kaşikçi 2012) and comorbid conditions (Molloy & O'Carroll 2017). Given the differing national contexts and variation in the sociodemographic characteristics between the Australian and Iraqi groups, differential effects might have been anticipated. However, no sociodemographic or health related factors retained significance in multivariate modelling to predict medication adherence. The similarity of the findings from the two countries are striking; despite their very different cultures, independently predictive variables showed little difference. Further research is required to fully understand the perceived barriers to refilling medication, detail of beliefs and confidence to take medication.

Study findings indicated that the location of recruitment in relation to CVD services (cardiac ward versus cardiac clinics, a proxy for differing time points in the cardiac patient journey) was a significant predictor of medication adherence among Iraqi patients, with more participants from the cardiac ward having medium/low adherence than those recruited as out-patients. It might have been anticipated that patients admitted for an acute cardiac event might report worse medication adherence than patients seen as out-patients, who might reasonably be expected to be more clinically stable. However, this pattern was not seen in patients recruited in Australia. No research has previously examined the relationship between cardio-protective medication adherence and service provider location/cardiac patient journey time point in Iraq, where poor adherence with cardiovascular medications might be attributed to CVD service deficiencies both for in-patients and out-patients (Kronish & Ye 2013). Another possible explanation might be that patients' opportunities to attend cardiac clinics were less in Iraq, with those attending being generally more motivated, perseverant, and willing to attend follow-up with their cardiologists, with consequently relatively better medication adherence (Bedell et al. 2000). Perhaps more medication education was delivered in the out-patient clinics than in the cardiac wards in Iraq, but with less variation in Australia. The study findings highlight the importance of patient education and medication related knowledge to enhance adherence behaviour in cardiac ward before patient discharge, in out-patient clinics and cardiac rehabilitation settings (Curl et al. 2016). Iraqi patients with CVD might have experienced particular problems in accessing quality health services due to the lack of or limited resources which might include provision of medications in public hospitals. This study reveals the need for nursing educational interventions to not only educate patients on their medications and send out reminders but also address patients' beliefs about their medications and their ability to self-administer and refill medications.

4.8 Limitations of the Study

This study is attended by a number of limitations. Although medication adherence self-reports are useful and have been shown to be reasonably accurate measures of medication adherence, this approach can be susceptible to information and social desirability bias (Morisky & DiMatteo 2011). Further, our adherence measure did not distinguish between specific cardiac medication classes but rather medication adherence behaviour generally (Crowley et al. 2015). For many of those tools, particularly the MAQ, there are to date only limited validation and reliability data available, which may limit confidence in their ability to accurately indicate patients' adherence to their medications. Cardiac patients' beliefs about medication and their ability to refill cardiac medication may have been influenced by the type of cardiac medications taken by study participants due to differences in side effects and cost. The differences in sociodemographic characteristics and some health-related variables between Australian and Iraqi samples may limit the interpretation of the comparative findings. Future research should include and recognise different classes of cardiac medications. The adequacy of the statistical power to detect subgroups differences was not assessed, but this was not the primary aim of the study. Data were collected utilising convenience sampling from three different hospitals in Iraq and one hospital from Australia. Convenience sampling from multiple sites may have allowed the sample to better represent these populations with regard to demographic characteristics. Further investigations are needed to confirm the predictive power of the model and to explore causation paths to medication adherence. Further studies are required to consider the internal and external validity of the predictive model and report on the measurement of predictive performance. Finally, longer term follow-up would add valuable information about the sustainability of medication adherence behaviours across the cardiac patient journey.

4.9 Conclusion

The findings of this cross-sectional study are unique in terms of comparing cardiac medication adherence behaviours between patients from developed and developing countries: Australia and Iraq. The study results sought to inform new behavioural nurse-led approaches to improve medication adherence in patients with CVD. For the future such behavioural interventions should include ability to refill medications and address medication-related beliefs to encourage medication adherence. Further follow up study is needed in both Australia and Iraq, where strategies should be tailored to target these factors that have been shown to predict patients' adherence behaviours across cultures and settings/disease time points. New interventions are urgently required to improve the unacceptably poor medication adherence in both Australia and Iraq.

The findings of this study have crucial implications for nursing practice, education, policy and future research. Findings indicate that nurses should focus on exploring patients' beliefs about their medications and promote accurate knowledge of cardiac medications. This should also include a focus on ability self-administer and refill medications, taking into account individual and local situations and contexts, including, for example, the geo-political situation of the Middle East. A predictive model was built to examine factors associated with medication adherence in cardiac patients recruited from Australia and Iraq. The model provides a better understanding of the patients' future medication adherence behaviours by identifying distinct and measurable data from these two countries.

Nurse can use study findings to inform development and implementation of nurse-led interventions to enhance cardio-protective medication adherence in Australia and Iraq, with clinical and cost-effectiveness outcomes informing clinical practice. Such interventions should address the principal behavioural causes of sub-optimal adherence especially patients' belief about medication and their ability to correctly self-administer and refill medications. They should enable nurses to strengthen patients' knowledge and beliefs through motivational consultations, education and information sessions. Future research is recommended to explore predictors of medication adherence in greater depth and in broader CVD populations in both Australia and Iraq. Nurse-led interventions developed to apply study findings should be the subject of future trials in Australia and Iraq. The information provided by this study can support development of behaviour change interventions delivered by nurses across a wide range of cultures and settings and time points in the CVD journey.

4.10 Summary

To our knowledge, this is the first comparative study to report and compare adherence to cardiac medications and associated factors in patients with CVD at different points in the cardiac disease trajectory in Australia and Iraq. Significantly more participants from Iraq reported medium/low levels of adherence to their cardiac medications compared to participants from Australia. This study revealed that patients' ability to correctly self-administer and refill their medications and beliefs about medications were significantly predictive of their reported adherence behaviours in both Australia and Iraq. In Iraq, location of recruitment (cardiac ward versus cardiac clinics; a proxy for two different time points in the CVD journey: following an acute event and during stable self-management) was significantly predictive of patients reported adherence behaviours. The information provided by this study will therefore be potentially suitable to support behaviour change interventions across a wide range of settings and time points in the CVD journey. The following chapter synthesises the information provided by chapters two, three and four in presenting the published protocol of a multi-methods study including a pilot randomised controlled trial intended to evaluate the effectiveness of nurse-led, multi-faceted intervention to enhance medication adherence in patients with CVD. The protocol examines the role of individual, behavioural and environmental factors in predicting medication non-adherence in patients with CVD.

CHAPTER 5 Behaviour Change Interventions to Improve Medication Adherence in Patients with Cardiac Disease: Protocol for a Mixed Methods Study Including A Pilot Randomised Controlled Trial

5.1 Introduction of the Chapter

This chapter is based on a paper published in Collegian (Al-Ganmi et al. 2018) – see **Appendix L** for publication: Al-Ganmi A.H.A., Perry, L., Gholizadeh, L. & Alotaibi A. (2018). Behaviour change interventions to improve medication adherence in patients with cardiac disease: Protocol for a mixed methods study including a pilot randomised controlled trial. Collegian, 25(4). 385–394.

This chapter describes the research design and methods used for a mixed-methods study including a pilot RCT. It outlines the research paradigm guiding the development of the protocol for the pilot RCT study and the rationale for future use of mixed methods to conduct the data collection and analysis. The design and reporting of the trial protocol were undertaken using the CONSORT guidelines. The study design was planned based on the results of the systematic review published in Journal of Advanced Nursing. The chapter also outlines the potential setting for the study, its sampling methods and recruitment and the instruments proposed to collect and analyse quantitative and qualitative data. In addition, the strategies applied to enhance the validity, reliability and rigor of the study are outlined and the ethical considerations discussed. This chapter proposes a randomised controlled trial (RCT) to pilot-test the hypothesis that a theory based, nurse-led, multifaceted intervention comprising motivational interviewing techniques and text message reminders in addition to standard care will better promote medication adherence in cardiac patients compared to standard care alone.

5.2 Introduction

World-wide, the prevalence of cardiovascular disease (CVD) is increasing rapidly because of changes in population lifestyles (Hauptman 2008), resulting in major concerns for community health (Zhu et al. 2015). Cardiovascular disease has emerged as a leading cause of death and disability in Australia (Nichols et al. 2014), affecting one in six people and responsible for 16% of the nations' total disease burden. It is the main reason for rehospitalisation (Australian Institute of Health and Welfare 2014); costs in 2004–2005 of AU$5.94 billion accounted for 11% of Australia's total health expenditure (Australian Institute of Health and Welfare 2010). Quality of life has been shown to improve for patients with CVD referred to a comprehensive cardiac rehabilitation and secondary prevention program (Shepherd & While 2012). These programs comprise recovery and preventative activities aimed at modifying cardiac risk factors and enhancing physico-psycho-social function to reduce the risk of subsequent cardiac events (Woodruffe et al. 2014). Cardiac rehabilitation enables changes in patients' lifestyles by providing education and skill development to reduce cardiovascular risk factors, and to promote adherence to prescribed medications.

Prescription medications, an important form of secondary prevention for CVD, have been a key factor in the 20% reduction seen in mortality rates within one year of diagnosis of acute myocardial infarction (AMI) (Chase et al. 2016); and the 28% reduction within three months of AMI between 2006 and 2007 (Kolandaivelu et al. 2014). While cardiac medications have been shown to be effective for symptom management and slowing the progression of CVD, consistent adherence to prescribed medication regimes is required to achieve these effects (Hunt et al. 2009).

The World Health Organisation (WHO) defines adherence as 'the extent to which a person's behaviour (taking medications, following a recommended diet and/or executing lifestyle changes) corresponds with the agreed recommendations of a healthcare provider' (Sabaté 2003). Adherence to medications is a challenge, particularly for patients with cardiac disease who often require multiple medications for prolonged periods (World Health Organisation 2003). The risk of mortality and morbidity in such patients increases if adherence to prescribed medication is suboptimal (Hope et al. 2004); yet reported rates of non-adherence vary from 33% to more than 50% (Munger et al. 2007, Li et al. 2012, Shah et al. 2013), contributing to increased numbers of CVD-related Emergency Department visits, hospitalisation, reduced health and well-being, augmented healthcare costs and risk of death (Mukhtar et al. 2014, Whittle et al. 2016). It is therefore important to identify the factors that influence medication adherence (Munger et al. 2007) and provide tailored interventions to improve patients' medication-taking behaviours (Santo et al. 2016).

5.3 Background

Medication adherence is linked to better clinical outcomes among patients with heart disease, reducing the risk of hospital readmission and death (Ruppar et al. 2016). Suboptimal medication adherence is a multidimensional issue. Socio-economic and patient-related factors include low educational levels, inadequate knowledge about disease and medications, beliefs about medications and patients' motivation to manage their illness and improve their overall health (Broekmans et al. 2010). Lack of social support and psychological, cognitive or medical vulnerability can also play a part (Kronish & Ye 2013). Factors shown to predict medication non-adherence include low self-efficacy, attitudes and beliefs about medications, low perceived behavioural control, and lack of social support (Morrison et al. 2015). Patients with concerns about their medications are more likely to report forgetting to take them or intentionally skipping doses (World Health Organisation 2003). Older people and people in poor health or with co-morbidities are less likely to successfully self-administer (Krueger et al. 2015). Medication self-efficacy and beliefs about medications may also influence the adoption and maintenance of medication adherence behaviours (Bane et al. 2006), and these factors can be affected by psycho-social factors such as the perceived level of social support and mood (Cha et al. 2008).

Exploring patients' emotions and beliefs while helping to strengthen their self-efficacy may minimise barriers to behavioural change and motivate them to adhere to their medications (Riegel et al. 2016). It is important to promote behavioural change by exploring what drives an individual patient to make changes or to maintain the status quo. This can be achieved by applying motivational interviewing techniques that have been found to be effective in assessing a patient's readiness to change and subsequently moving toward change at an appropriate time (Dart 2010). Motivational interviewing has been shown to be effective in increasing medication adherence in cardiac patients (Ogedegbe et al. 2008). Also, text messages have been effective in improving the use of prescribed cardiac medications among 65% of patients at six months (Wald et al. 2014). Understanding the reasons for poor adherence may suggest approaches to novel interventions.

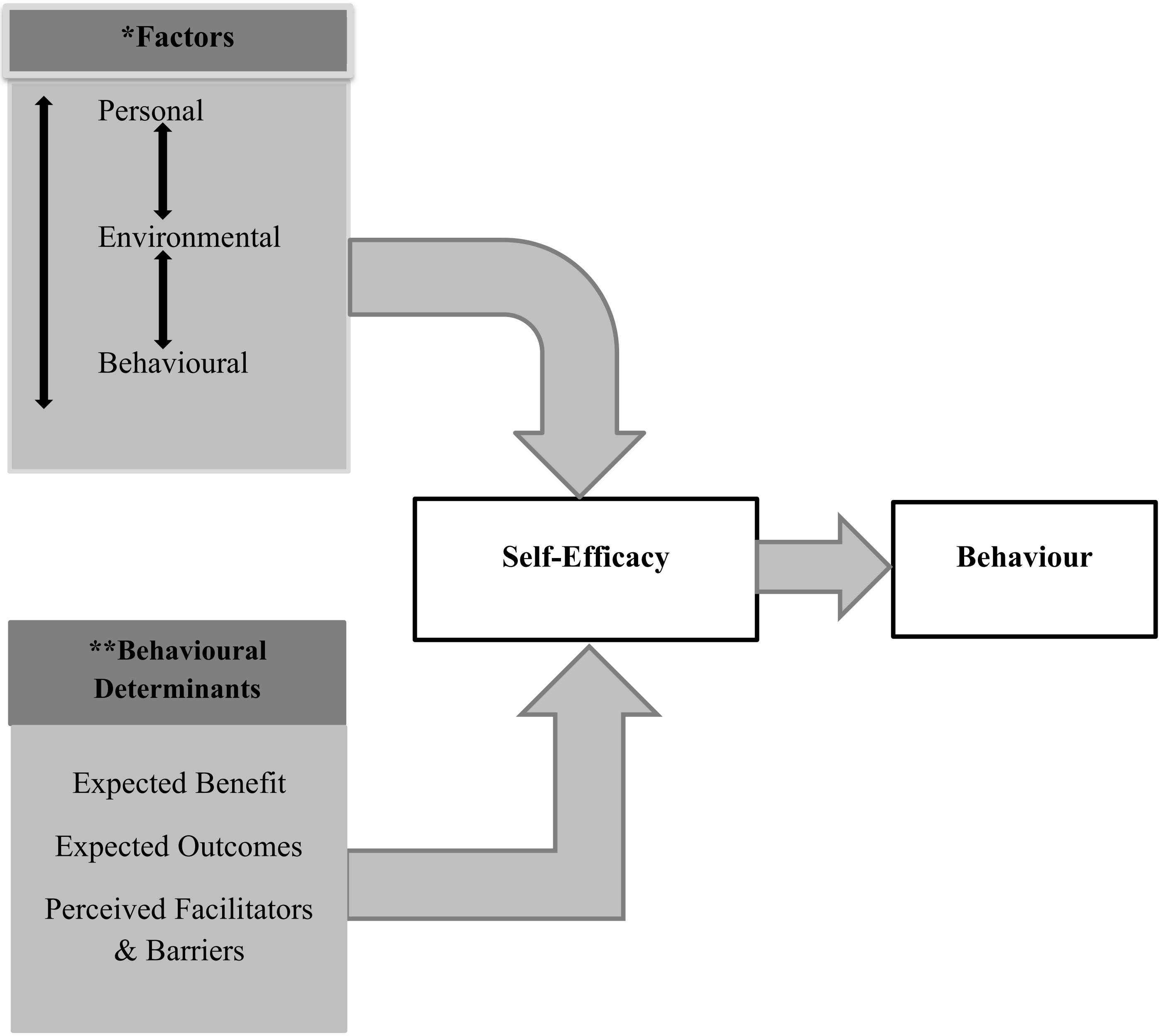
5.4 Theoretical Framework Guiding the Study

This study will use Bandura's social cognitive theory to enhance the refinement of self-efficacy (Bandura 1977) and to examine the effects of individual, behavioural and environmental factors on medication adherence. According to the theory, self-efficacy is the pivotal determinant in influencing a person's particular behaviour, directly affecting one's actions and impacting on other determinants (Bandura 1977, Bandura 2004). Bandura (2004)) notes that self-efficacy determines the expected outcomes of people's behaviours. Reciprocal determinism is the basic organising principle of behaviour change proposed by this social cognitive theory, with continuous, functional interaction between the environment, the individual and behaviour (Bandura 1998) (**Figure 5.1**). It assumes that a change in knowledge of health risk and benefits is essential, but requires additional impacts for change to occur (Munro et al. 2007). Other determinants of behaviour change include behaviours, outcome expectations, expected benefits, beliefs and goals, and perceived facilitators and barriers. The theory proposes that if people perceive that they have outcome control, appropriate behaviour will follow, with sufficiently high self-confidence to overcome otherwise insurmountable barriers (Armitage & Conner 2000).

Other theoretical approaches, including the Theory of Planned Behaviour (TPB), are also commonly applied to develop insights on the determinants of behaviour. The SCT is a particularly useful model to consider when healthcare providers are counselling patients with chronic health conditions such as CVD, as it focuses on empowerment for self-management and to effect change. SCT can be used to assist patients in enhancing their knowledge about CVD and potential actions to take in making decisions about the disease and its associated health challenges, such as medication adherence (Adefolalu 2018). To support patients with CVD, cognitive and behavioural strategies can be used to empower patients to negotiate problems around medication adherence and establish supportive relationships which strengthen patients' ability to adhere to their medication regimes. This should subsequently lead to better adherence and improve clinical outcomes. While SCT suggests that knowledge of health risks and benefits is a prerequisite to change, additional influences are necessary for change to occur (Munro et al. 2007), such as self-efficacy, outcome expectations, expected benefits, perceived beliefs, goals, and perceived facilitators and barriers. Hence, this theory proposes that behaviours are enacted if people perceive they have control over the outcome, that there are no insurmountable external barriers and when individuals have confidence in their ability to execute the behaviour (Armitage & Conner 2000).

Using a theoretical basis to explain relationships between study variables is important when designing effective behavioural change studies (Short et al. 2013). Appropriately designed interventions that employ multiple strategies, such as motivational interviewing to encourage behaviour changes and text messaging strategies to reinforce behaviours, are likely to achieve significant increases in medication adherence in cardiac patients (Al‐Ganmi et al. 2016).

Figure 5.1 Synthesis of *Social-Cognitive and **Self-Efficacy Models (Bandura, 1998) Guiding the Intervention of this Protocol.



5.5 Methods

5.5.1 Aims and Hypothesis

This study part of the thesis aims to use a pilot randomised controlled trial (RCT) to test the hypothesis that a theory based, nurse-led, multi-faceted intervention comprising motivational interviewing techniques and text message reminders in addition to standard care will better promote medication adherence in cardiac patients compared to standard care alone. Underpinning evidence and assumptions of the hypothesis are that:

1) A high proportion of patients fail to adhere to their cardiovascular medication regimes.

2) The baseline assessment of medication adherence in patients with CVD may increase their health-consciousness, which may trigger the initiation of changes in their behaviour regarding medication adherence, especially when they know or recognise that they have low medication adherence.

3) Medication adherence self-efficacy, patient beliefs, and lack of social support are predictive factors associated with non-adherence to medication.

4) High quality evidence supports the use of multi-faceted interventions comprising of motivational interviewing counselling combined with text messaging reminders to promote medication adherence.

5) Medication adherence assessment, using a collaborative communication style, the patient's own expressions and responding to their cues, may be an effective means to understand their adherence problems and set goals to improve their medication adherence behaviours.

The pilot study will assess self-reported adherence or non-adherence to cardiovascular medication in patients referred to a cardiac rehabilitation program following hospital admission for an acute cardiac event and test the feasibility of the intervention. Medication non-adherence has been defined as ‘taking less than 80% of prescribed doses and can also include taking too many doses’ and it is associated with an increased risk of poor health, adverse clinical events and death (Nieuwlaat et al. 2014). The study will examine the role of individual, behavioural and environmental factors in predicting medication non-adherence in patients with CVD.

5.5.2 Study Design

This is a mixed methods study which includes a nested, pilot RCT. Both qualitative and quantitative methods are required to address the study’s aims and hypothesis. The use of mixed methods is valuable to provide a fuller picture of the topic and to transcend the limitations of each of the methods used singly (Borkan 2004, Creswell et al. 2004).

In this study, data collection will occur sequentially: quantitative data collection followed by qualitative data collection will occur for the exploratory phases that will provide the explanatory power in support of the final (RCT) intervention testing phase: (QUAN + qual) → QUAN. Results from the exploratory phases (survey design and semi-structured interviews) will inform the fine tuning of the intervention in the third phase.

This multi-method study will entail three interrelated phases:

Phase one: The survey is designed to identify cardiac patients’ patterns of medication adherence and their associated degree of adherence. The purpose of the survey is to gather quantitative data about medication adherence, patient behaviours, beliefs and other associated factors, including demographic data (**Appendix F**) which will inform intervention and form baseline data.

Phase two: A descriptive qualitative study will explore the phenomena of cardiac patients' adherence to medications and how they respond to factors that affect medication adherence. Using semi-structured interviews, patients' views of their cardiac medications will be explored as well as the factors that influence their medication adherence.

A semi-structured interview format was chosen because of its flexibility in collecting self-reporting data (Cohen & Crabtree 2006), enabling participants to talk freely about issues related to their medication adherence and telling stories in their own words. Semi-structured in-depth interviews will involve open-ended questions to elicit detailed narratives and stories (Whiting 2008). This will provide in-depth understanding to supplement and explain quantitative results from Phase one.

Details of Phase one and Phase two data will be used to inform motivational interviewing techniques and to tailor the interventions to individual patients' needs to better support their adherence to cardiac medications.

Phase three, a pilot RCT: Participants identified as non-adherent to their medications in Phase one (based on Medication Adherence Questionnaire [MAQ] scores) and Phase two data (themes and patterns of medication adherence/non-adherence) will be invited to take part in this pilot trial. This will pilot test the feasibility and effectiveness of a multi-faceted intervention strategy, including motivational interviews plus text message reminders, to influence adherence to their cardiac medication regimes. The RCT will test and compare differences in outcomes between the standard care delivered by a cardiac rehabilitation program and the same program augmented by this multi-faceted intervention. The feasibility of conducting a multi-faceted behavioural intervention in a busy cardiac rehabilitation setting will be investigated. We also sought data to determine the effect size for sample-size calculation as we could only extrapolate an estimated effect size from a somewhat similar trial for the sample size calculation of this pilot study. Data are currently lacking for full-scale trial of this approach among cardiac rehabilitation patients.

5.5.3 Study Setting and Participants

The study will be carried out in the cardiac rehabilitation centre of a tertiary referral hospital in Sydney, Australia. Participants will be cardiac patients referred to a cardiac rehabilitation program following their admission for an acute cardiac event; those participating in the pilot trial will be randomly allocated to receive either the intervention plus standard care or standard care only. Inclusion criteria are: 18 years of age or older; diagnosed with cardiac disease and referred to the hospital cardiac rehabilitation program; and currently taking at least one cardio-protective medication and having primary responsibility for taking their own medications (i.e. not reliant on a carer). Participants must be able to read, speak and understand English, have a personal mobile phone, and be able to receive and reply to phone calls and text messages. Patients who are blind, deaf or unable to consent to receiving text messages will be excluded. Those clinically judged to have cognitive impairment that limits their ability to understand and answer the study questions will also be excluded.

5.5.4 Sample Size Determination

The sample size for the pilot RCT was based on data from Ma et al. (2014)). Using a two-sided test, moderate effect size with $\alpha = 0.05$, and power = 0.80, nine participants are required in each group. Allowing for 50% loss, a total of 28 cardiac patients will be needed for the pilot RCT.

Around 350 patients per year (30 per month) are estimated to attend the cardiac rehabilitation centre. Pilot data indicate around one third are considered non-adherent to medications. If 50% of eligible patients agree to participate, recruitment will progress at five participants per month (a rate of recruitment easily manageable for the researcher): it will take six months to enrol 28 participants, so the study will take approximately six months for recruitment and six more months for intervention and follow-up.

5.5.5 Study Procedures and Data Collection

Data collection will take place at baseline and at six months, and changes in medication adherence will be compared within and between groups to determine any intervention effect. The Consolidated Standard of Reporting Trials (CONSORT) diagram of study processes is presented in **Figure 5.2**. Baseline survey and interview data will be collected during patients' hospital attendance for a cardiac rehabilitation session. Pilot RCT participants will repeat the Phase one survey via telephone interview at six months post-randomisation to collect the follow-up data; three additional open-ended questions (**Appendix I**) will explore participants' experiences of the motivational interview and the text messaging and enquire whether anything else might have helped adherence.

In Phase two each interview will involve a face-to-face meeting for an interview guided by a set of questions or topics (Polit & Beck 2004). Interviews will be arranged with participants using preferred communication methods with reminders two days beforehand. The guide for the individual semi-structured interviews can be found in **Appendix J**. Data collection, transcription and analysis will be conducted, with questions modified in light of responses and emergent themes (Braun & Clarke 2006).

5.5.6 Recruitment, Enrolment and Consent

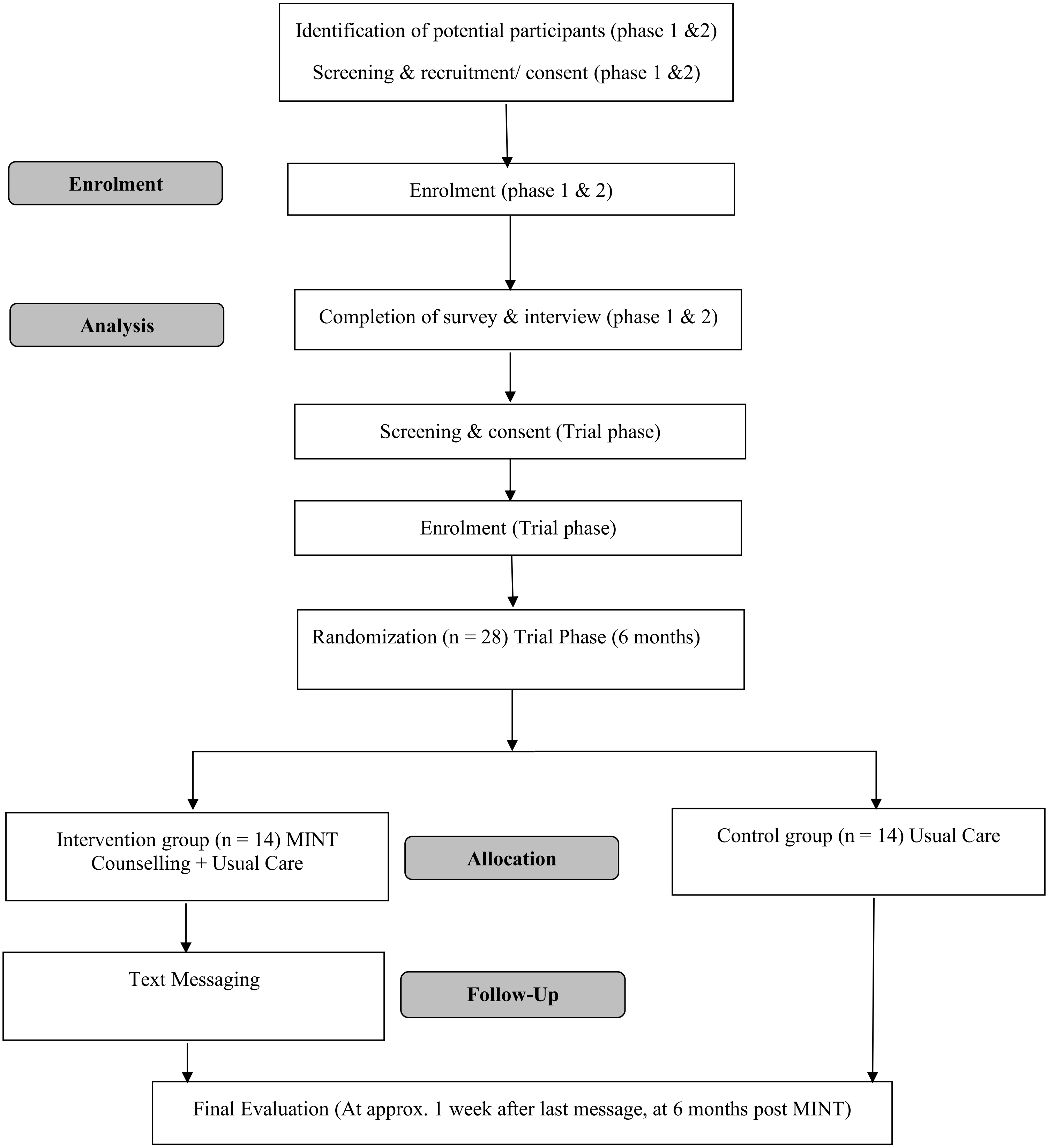
Recruitment will occur under the supervision of the clinical nurse consultant for cardiac rehabilitation, with the agreement of the director of nursing and the cardiology consultant. Patients referred to the cardiac rehabilitation program will be screened using the study inclusion/ exclusion criteria by the clinical nurse consultant at their first session. Eligible members of a consecutive cohort of patients who express interest in the project will be referred to the researcher, who will explain the study phases and provide an information statement and consent form. Completion of the survey will identify patients who are non-adherent with at least one cardiac medication, based on their answers to the MAQ with their non-adherence confirmed and detailed at Phase two by semi-structured interview (Sieben et al. 2019). Any discordance in responses across the two phases was discussed with the participants during the interviews. At the conclusion of the semi-structured interview (Phase two), eligible participants will be informed about Phase three, the pilot RCT, and invited to participate.

The researcher will obtain written informed consent from participants for Phases one and two; similar consent to participate in the pilot trial will be obtained separately. Participants will receive a folder at enrolment, including written information about the study and a copy of their consent form, to supplement the face-to-face explanation of the study.

5.5.7 Randomisation and Blinding Processes

In the pilot RCT, participants will be randomly assigned to either intervention or control group after they have consented to the trial phase. A computerised random number generator will be used to generate the random sequence. Using permutated blocks equal numbers of participants will be assigned to each group. Sequentially numbered sealed envelopes will be used to conceal the sequence until participants are assigned. Neither the participants nor the researcher can be blinded to the group allocation because of the nature of the behavioural intervention. A behavioural intervention such as motivational interviewing is not easily delivered blinded, and it is unlikely that cardiac patients in a cardiac rehabilitation program would not know which intervention they are receiving (Page & Persch 2013). Outcome data are self-reported, but the assessor who will collect the outcome data will be blinded to study allocation to reduce potential bias.

Figure 5.2 Recruitment Flow Diagram for this Protocol Based on the CONSORT Schematic



5.5.8 The Study Intervention

Approaches such as motivational interviewing aim to encourage behaviour change through influencing individual's feelings, thoughts, and confidence to change their behaviours, for example: adhere to a recommended medical regime. The technique facilitates behaviour change by resolving patients' ambivalence to change (Miller & Rollnick 2002). Motivational interviewing has been incorporated into several successful medication adherence interventions (Solomon et al. 2009). Using this technique, a wide variety of medication non-adherence factors are targeted, enabling patients to reflect on perceived barriers and search for solutions (Easthall et al. 2013). The interviewing 'elicits a range of possible actions and affirms the patient's autonomy to make informed choices' (Riegel et al. 2016). Self-efficacy, one of the targeted factors, predicts adherence to medications, and this may be mediated by patients' beliefs about their ability to cope, to locate optimistic changes in their social relations and to improve their individual confidence (Luszczynska et al. 2007). Social cognitive theory has previously been applied to examine medication adherence among CVD patients (Haskell et al. 1994), to foster individuals' medication adherence by setting goals and creating firm commitments to them, thereby encouraging patients to exercise more control over behaviours. In turn patients can come to believe they have a higher ability to adhere to their medications (Smith et al. 2003).

Text messaging has been widely used to improve health behaviours across multiple diseases (Spoelstra et al. 2015). It has been used to improve medication adherence by affecting different elements of cognition and evoking attention and an automatic response (Yiend 2010). Text Messaging is widely available low-cost, patient friendly, requires low technological expertise and is applicable in a diverse range of health behaviours, acting as a safety-net for medication reminders (Cole-Lewis & Kershaw 2010, Zallman et al. 2016).

5.5.8.1 Intervention Arm

Participants in the intervention group will receive current standard care through the cardiac rehabilitation program plus behavioural counselling about medication adherence using motivational interviewing and text reminders. The current cardiac rehabilitation program includes a single one-hour information session on cardiac medication. The content received by both group participants will be recorded and compared to check for equivalence between the groups.

Each patient in the intervention group will receive approximately 30 to 40 minutes of a single motivational interview-style counselling session (Ma et al. 2014). The essence of motivational interviewing is for the counsellor to be simultaneously sympathetic and supportive, as well as directive in moving patients toward behaviour change by strengthening their reasons to change (Levensky et al. 2007). As part of the counselling, the researcher will provide information that the patient may need, and explore barriers that keep the patient from adhering to the medication regime (Dart 2010). A structured counselling script will be designed that can be tailored to medication adherence characteristics of individual patients (Dart 2010). Examples of the content of the session are available in **Appendix K**. The sessions will be audiotaped and reviewed by a clinician qualified in motivational interviewing to ensure fidelity (Ma et al. 2014).

Text message reminders will be sent daily for the first two weeks, then on alternate days for fortnight, then once a week for the next five months, for a total of six months (Wald et al. 2014). The content will vary according to each patient's non-adherence factors. Examples are supplied in **Table 5.1**.

Table 5.1 Examples of Text Message Reminders

Example 1	'Hello Mr/Mrs………… Have you refilled your heart medication? Please text Y if you refilled your medication before receiving this text, text R if your answer is the message has reminded you and you will refill your medication; text N if your answer is No. Thank you.
Example 2	Hello Mr/Mrs………….. Have you taken your heart medication today? Please text Y if you took your medication before receiving this text, text R if your answer is the message has reminded you, and you will take your medication; text N if your answer is No. Thank you.
Example 3	Hello Mr/Mrs………… Have you arranged to take your heart medication more than once today? Please text Y if your answer is you have arranged to take your heart medication twice a day before receiving this text; text R if your answer is the message has reminded you; text N if your answer is No. Thank you.

5.5.8.2 Control Arm

For the period of the study, patients in the control arm will be provided only with current standard care, which includes the provision of cardiac care knowledge and recommendations to enhance medication adherence and to promote healthy lifestyles; they will complete the same surveys as the intervention arm at baseline and at six months.

5.5.9 Outcomes

The primary outcome is medication adherence/ non-adherence at six months. Medication adherence will be determined based on participants' responses to the MAQ (Morisky et al. 1986). Patients with a sum score of 1–2 will be considered 'adherent'; those with a score of 3–4 as 'non-adherent' (Morisky et al. 1986).

Secondary outcomes include identification of those factors exerting a significant influence on medication adherence, such as behaviour (self-regulation), beliefs (general harm; general overuse; specific necessity; and specific concerns), social support and self-efficacy using a combination of instruments, outlined below.

To assess the acceptability of the intervention at six months, the researcher will telephone each member of the intervention group to evaluate their experience of the interview and text messages (**Appendix I**).

5.6 Study Instruments

The survey will include a set of questionnaires designed to gather data about medication adherence and patient behaviours, beliefs and other factors associated with adherence/ non-adherence. The survey will be paper based, self-administered, and suitable for participants with low literacy skills. Sociodemographic and health data will be collected: age, gender, living arrangement, level of education, ethnicity; co-morbidities.

The use of different instruments in this study will enable comprehensive study of factors contributing to medication non-adherence in patients with CVD, including behavioural and psychological factors. Motivational interviews in the RCT phase will focus on the identified non-adherence factors for each individual patient.

Medication non-adherence will be assessed by the Medication Adherence Questionnaire (MAQ) (Morisky et al. 1986), which is designed to measure medication adherence behaviour and barriers such as forgetfulness, carelessness, adverse effects and efficacy. It includes four simple dichotomous questions, assigning one point for each yes response;

total scores are categorised as: 0 = high; 1–2 = medium, and 3–4 = low medication adherence behaviours (Morisky et al. 1986).

The Adherence to Refills and Medications Scale **(**ARMS) (Kripalani et al. 2009) will be used to determine medication adherence behaviour in terms of self-regulation. The ARMS is a 12–item scale: an eight-item medication-taking subscale assessing correct self-administration for the prescribed medications; and a four-item prescription refill subscale evaluating the patient's ability to replenish medications on schedule. Each item is scored on a four-point scale ranging from l = none of the time to 4 = all the time on a 4-point Likert scale, with higher numbers demonstrating better refill ability for medications on schedule (Kripalani et al. 2009).

The Belief about Medicine Questionnaire (BaMQ) (Horne et al. 1999) elicits information on patients' beliefs about medications which may be adherence-related. It identifies whether the patient believes in the necessity of their medicines or has concerns about them. The study will use the short (eight-item) version of the BaMQ developed by Horne et al. (1999), composed of four subscales of two items each, assessing: specific necessity, specific concerns, general overuse and general harm. Answers range from l = strongly disagree to 5 = strongly agree on a 5-point Likert scale; scores are summed to derive a total score, with higher scores indicating more positive beliefs.

The Medication Adherence Self-Efficacy Scale-Revised (MASESE-R) (Fernandez et al. 2008) consists of 13 items that evaluate an individual's ability to adhere to medications under various challenging circumstances. Twelve items examine patients' confidence in taking medications in specific circumstances (e.g. with family, in public places, feeling well), and one assess the ability to take medications as part of the everyday routine. Each item is scored on a 4-point Likert scale, ranging from 0 = not at all sure to 3 = extremely sure. A single score is derived from the mean of all items, with greater self-efficacy indicated by high scores (Fernandez et al. 2008).

The Medication Specific Social Support (MSSS) scale (Lehavot et al. 2011) is an eight-item survey of medication-specific social support to identify how often others help patients with their medication, scored for each item ranging from 0 = never to 4 = very often. A single mean score is presented as a medication-specific index of support (Lehavot et al. 2011).

5.6.1 Validity and Reliability

The MAQ is a validated four-item tool suitable for a wide range of conditions involving cardiac diseases (Nguyen et al. 2014). Its validity and reliability has been determined in patients with hypertension, with a reported acceptable internal consistency of $\alpha = 0.61$, sensitivity 0.81 and specificity 0.44 (Lavsa et al. 2011); it has also been validated in patients with heart failure, CVD and dyslipidemia (Afonso et al. 2006). MAQ score was found to be a significant independent predictor of cardiovascular nonadherence in a multivariate logistic regression model (Shalansky et al. 2004) (**Table 5.2**).

The ARMS subscales are highly correlated with the Morisky medication adherence four-item scale, and with medication refill adherence (Kripalani et al. 2009). The ARMS has been validated in patients with cardiovascular disease and other chronic diseases (Kripalani et al. 2008). Among patients with low literacy skills (Kripalani et al. 2009) it has demonstrated high internal consistency using Cronbach's α and test–retest reliability, set out in **Table 5.2** (Kripalani et al. 2009).

Table 5.2 The Reliability and Validity of Study Instruments

Questionnaire	Validity	Reliability
Medication Adherence Questionnaire (MAQ) (Morisky et al. 1986).	➢ Validated in patients with hypertension (sensitivity and specificity were 0.81 and 0.44. respectively) (Morisky et al. 1986), dyslipidaemia (Afonso et al. 2006), heart failure (George et al. 2000), and CAD (Shalansky et al. 2004). ➢ There was a moderate correlation between the MAQ score & percentage adherence with cardiovascular medications as assessed by prescription refill records (r –0.30; $p < 0.001$) (Shalansky et al. 2004). ➢ MAQ score was a significant independent predictor of cardiovascular nonadherence by multivariate logistic regression (CI: 0.7 to 0.9; $P < 0.001$). ➢ MAQ demonstrated concurrent validity with blood pressure control at baseline (low score 42%, compared to 54% for patient who scored high).	Cronbach's ɑ = 0.61
Adherence to Refills and Medications Scale (ARMS) (Kripalani et al. 2009).	➢ Validated in patients with CAD & other chronic diseases (Kripalani et al. 2009). Psychometric analyses revealed high internal consistency, test–retest reliability, & criterion-related validity for ARMS. ➢ The ARMS test–retest reliability was assessed using Spearman's correlation coefficient. Correlations ranging from 0.7 to 0.9 are considered very good. ➢ Scores on the ARMS & its subscales correlated significantly with other measures of medication adherence-the four-item scale by Morisky and colleagues (Spearman's rho =–0.651, $P < 0.01$), & medication refill adherence.	Cronbach's ɑ = 0.81
Belief about Medicine Questionnaire (BaMQ) (Horne et al. 1999)	➢ BaMQ significantly correlated with other adherence scales: MAQ, Morisky Medication Adherence Scale (MMAQ), & medication adherence rating scale (MARS–5). ➢ Evidence for the validity of BaMQ domains was used by the General Medical and Cardiac samples (p= 0.5. n= 211, p < 0.00 1). ➢ BMQ was developed from a study in older individuals with multiple illnesses by reducing the original questionnaire to the best-discriminating items for the four BMQ subscales (two items each): General Harm (e.g., "Most medicines are addictive," inter-item correlation= .44, p < .01); General Overuse (e.g., "Doctors use too many medicines," inter-item correlation = .64, p < .01); Specific Necessity (e.g., "My health, at present, depends on my medicines," inter-item correlation = .79, p < .01); and Specific Concerns (e.g., "My medicines disrupt my life," inter-item correlation = .56, p < .01) (Schu¨z et al. 2011).	Cronbach's ɑ = 0.70
Medication Adherence Self-Efficacy Scale-Revised (MASER-R) (Fernandez et al. 2008).	➢ MASES-R assessed against electronic medication adherence & correlated positively & significantly ($r = .20$, $p = .02$). ➢ MASES-R correlate positively with self-report adherence & MEMS & the score was higher at baseline for patients whose self-report categorised them as adherent ($M = 3.81$, $SD = .33$), compared to non-adherent ($M = 3.51$, $SD = .52$; $t = -4.26$, $p < .001$).	Cronbach's ɑ = 0.91
Medication Specific Social Support (MSSS) (Lehavot et al. 2011).	Not stated	Cronbach's ɑ = 0.92

The BaMQ has been shown to correlate significantly with other adherence-related questionnaires such as MAQ, the Morisky medication adherence scale, and the medication adherence rating scale (MARS-5) (Horne et al. 1999, Mårdby et al. 2007, Gatti et al. 2009). Each BMQ subscale has been evaluated for internal consistency using Cronbach's α (Horne et al. 1999). Demonstrating criterion-related validity, the four BaMQ categories correlated highly with patients' beliefs about the adverse effects of medication and specific concerns as assessed by the Sensitive-Soma Scale administered to general medical and cardiac groups (**Table 5.2**) (Horne et al. 1999).

The MASES-R has been found to correlate significantly with electronic medication adherence records (MEMS) at three months, confirming its predictive validity (Fernandez et al. 2008). The concurrent validity of the MASES-R has also been confirmed (**Table 5.2**).

5.7 Data Analysis

Phase one: Descriptive statistics will be used to analyse data related to the patients' baseline characteristics. Data will be checked and cleaned prior to entry into SPSS for Windows version 23. Measures of central tendency and dispersion will describe the values of medication adherence, medication adherence self-efficacy, and beliefs about medication. Bivariate analyses will be conducted to examine factors potentially associated with medication non-adherence. Factors and behaviours related to medication non-adherence will be examined by logistic regression. Two sided tests will be conducted with significance set at .05.

Phase two: Qualitative data will be analysed inductively using thematic analysis (Sim 1998). This approach will focus on recognising, analysing and reporting recurrent patterns (themes) and subcategories within the data (Liamputtong 2013). Simultaneous collection, transcription and analysis allows the researcher to build on emerging themes (Polit & Beck 2014). Data will be examined and compared to identify similarities and differences by reading and searching within transcripts and across the data set (Polit & Beck 2014). QSR NVivo software will be used to code and construct thematic analysis (Braun & Clarke 2006). A similar but separate process will be employed with the data collected in response to the open questions at six months.

Pilot RCT phase: Data will be analysed according to the intention to treat principles. Using survey and demographic data, the two groups will be compared at baseline and any differences taken into account during the outcome assessment. Paired samples t-test analysis will be used to test within-group differences on the medication adherence questionnaire scores (MSSS, MAQ, ARMS, BaMQ, and MASER-R), and independent sample t-test will compare the scores of the intervention and control groups. Multinomial regression analysis will be applied to identify variables that significantly influence adherence to medication, such as self-efficacy, beliefs, level of confidence, or social support. Variables exerting significant influence on medication adherence in bivariate analysis will be entered in the regression analysis, with significance set at $P<0.25$ for the preliminary bivariate analysis and $P <0.05$ for the regression analysis (Polit. 1996).

5.8 Ethical Considerations

Approvals to conduct this study were granted by the appropriate health district and university Human Research Ethics Committees in June 2016 (reference numbers: 16/085 (HREC/16/POWH/218; ETH16–0635). The study is registered as a clinical trial (ACTRN12616000910404) on .

5.9 Discussion

Patients with CVD often have multiple chronic illnesses requiring multiple prescriptions. Studies of long-term medication adherence outcomes are limited (Bansilal et al. 2016) although non-adherence is common in these patients and accounts for substantial morbidity and mortality (Albert 2008). Adequate medication adherence may help improve quality of life by improving disease outcomes (Luszczynska et al. 2007). Better medication adherence may be achieved with interventions that address the known multiple factors of non-adherence, including lack of patient knowledge of perceived benefits, the perceived harm of medications, poor medication management and inadequate social support (Calvert et al. 2012).

Medication adherence interventions for patients with CVD have been shown to be effective when delivered by nurses, who should play an active role in designing and applying such interventions (Albert 2008, Chase et al. 2016). A recent systematic review emphasised that cardiac rehabilitation and prevention programs should encompass a dedicated strategy for medication adherence; at present, the majority of these programs do not measure and report adherence outcomes appropriately (Santo et al. 2016). There is scope for medication adherence interventions using techniques focused on promoting behavioural change to become part of routine healthcare (Easthall et al. 2013). This study part aims to evaluate the effectiveness of theory-based, nurse-led, multi-faceted interventions for medication adherence in a robust pilot trial using a RCT design, in line with the findings and recommendations of the recent review of medication adherence interventions for this population by Al‐Ganmi et al. (2016)).

5.10 Limitations

This study has some potential limitations. Firstly, use of a multi-faceted intervention, while recommended as likely to increase the success of the intervention as a whole, challenges researchers to identify the contribution of the individual components. This study attempts to address this by seeking participants' experiences of each separate component of the intervention. This will provide valuable input on the patients' experience, a component not specifically addressed in the intervention development. Based on previous literature, little is known about the patients' involvement in the development of these interventions. Secondly, measuring medication adherence through self-reporting may introduce a response bias presenting potential problems with reliability. Also, social desirability bias is possible due to lack of blinding. Self-reporting is a commonly used method of outcome assessment for medication adherence as it is acceptable to participants and imposes a minimal burden. It also has the potential to explore medication adherence behaviour, adherence-related barriers and beliefs about medicines which may support beneficial medication adherence assessment in chronic disease management. Finally, participants are predominantly older adults who will be asked to spend 20–30 minutes answering 45 questions in Phase one (repeated at six months for participants in the intervention group) and 30–45 minutes in the Phase two interview. This may challenge their stamina, patience and tolerance.

5.11 Conclusions

Medication non-adherence among patients with CVD is a major problem. Multi-faceted medication adherence interventions comprising motivational interviews and text reminders may improve adherence to cardiac medication regimes by targeting individual behaviour change. This pilot study will provide important information about techniques appropriate for use by nurses to support medication compliance in their patients. Findings may support development of further trials of this intervention in out-patient cardiac care settings ahead of translation into routine clinical care. It may also be suitable for implementing in other healthcare areas and long-term patient groups.

If this and further trials are successful, important next steps will be to consider the potential for widespread roll-out, including training nurses in motivational interviewing techniques. Software compatible with organisations' routine data programs will be required for automatic delivery of text messages. The time requirement of the intervention will need to be considered for staffing rosters and patient appointments. A full cost-effectiveness analysis is therefore recommended.

This protocol sets out the essential first steps for what may be an exciting new development in the contribution of nursing staff to delivering a substantial benefit to a sizeable patient group where there is clear potential for significant improvement in adherence.

5.12 Chapter Summary

This chapter presented the methodological design of the pilot randomised controlled trial suitable to test the effectiveness of an evidence-based nurse-led intervention in promotion of medication adherence in patients with CVD. This will be the first prospective trial of a nurse-led medication adherence intervention to be conducted in a cardiac rehabilitation centre in Australia. The chosen study design, of a randomised controlled trial, sheds light on the advantages of counselling and educational programs delivered using motivational interviewing techniques and text message reminders to promote adherence to cardiac medication. The principle of concordance between patients and healthcare professionals is a crucial aspect of the relationship whereby, the emphasising will be on the patients perspective on valuing the service, and sharing approaches to medication adherence between patients and healthcare providers (McCann et al. 2008). This will have implications for future interventions conducted by nurses to improve medication adherence taking into account the cultural background of patients with CVD.

CHAPTER 6 Discussion

6.1 Introduction

This chapter presents a discussion of the overall contribution of this thesis, in which findings are analysed to enhance the understanding of the medication adherence of patients with CVD in Australia and Iraq, and the factors that predict adherence. The main findings are discussed in relation to the research aims and relevant literature, as set out in Chapters 1 and 2. The chapter starts with a summary of the key findings of each component of the work as set out in Chapters 2, 3, 4 and 5, and discusses them with particular focus on their relation to the sociocultural and economic differences between Australia and Iraq. This chapter also discusses the proposed protocol, designed to pilot an RCT as a suitable test of the effectiveness of an evidence-based, nurse-led intervention in promoting of medication adherence. The thesis as a whole is finally considered in relation to its strengths and limitations

6.2 Key Findings

This section briefly highlights and summarises the key findings of the study. In Chapter 2, the systematic review (Al‐Ganmi et al. 2016) findings suggested that nurse-led interventions that apply motivational interviewing and text or phone messaging offer promising interventions to improve medication adherence. In Chapter 3, the results of the survey conducted in Australia (Al-Ganmi et al. 2019, Paper revised and submitted to Nursing and Health Sciences) indicated that overall, more than one-third of the patients had low levels of adherence with patients attending cardiac rehabilitation reporting lower adherence than patients who had experienced an acute event and been admitted to a cardiac ward. Patients' ability to self-administer and refill their cardiac medications and their beliefs about the medications were significant predictors of cardiac medication adherence. In Chapter 4, an international comparative study (Al-Ganmi et al. 2019) showed significantly poorer adherence to cardiac medications in Iraqi compared to Australian cardiac participants. Once again, patients' ability to correctly self-administer and refill medications, and their beliefs about cardio-protective medications independently predicted cardiac medication adherence behaviours, in participants from both countries. Finally, Chapter 5 presented a proposal for a pilot RCT suitable to test the effectiveness of an evidence-based, nurse-led intervention in promotion of medication adherence in patients with CVD (Al-Ganmi et al. 2018).

6.2.1 Interventions to Enhance Cardiac Medication Adherence

Interventions that are effective in improving adherence to cardiovascular medication in patients with CVD should result in significantly improved treatment and health outcomes (Nieuwlaat et al. 2014). Chapter 2 presented the findings of a systematic review of studies that have examined the effectiveness of interventions that are amenable to delivery by nurses in improving the adherence of patients to their prescribed cardio-protective medications (Al‐Ganmi et al. 2016). The review demonstrated that various interventions have been reported to improve adherence to cardiovascular medications using educational or behavioural strategies, or a combination of both. Multi-component interventions tailored to address patients' health beliefs and behaviours were shown to be effective in improving adherence, including counselling strategies such as motivational interviewing (MI) and adjuvant techniques such as text message (TM) reminders (Al‐Ganmi et al. 2016). The included studies were conducted in developed countries, but none were from Australia or developing countries such as Iraq. Moreover, evidence of the effectiveness of nurse-led interventions was limited because of compromise to the quality of the research and uncertainty of the effectiveness of intervention components. The evidence was limited by weak methodological approaches, lack of adherence definition, varied intervention methods (multiple approaches versus single approach), and various chronic care settings (Olaiya et al. 2016). However, the benefit of a well-designed nurse-led intervention to improve medications adherence in patients with CVD was clear, in line with and supported by an earlier review (Verloo et al. 2017).

Nurses have a significant role in the trajectory of the journey of patients with CVD and contribute to recovery and secondary prevention of the disease. The suggestion that nurse-led interventions involving multiple components can be effective in enhancing adherence behaviours has been acknowledged in the broader literature related to medication adherence among patients with chronic conditions (Farmer et al. 2012). Modes of intervention vary, and include counselling (Simoni et al. 2011), education sessions (Cutrona et al. 2010), and reminder strategies (Huber et al. 2017); findings in relation to all these approaches have indicated that such interventions can be efficient and reduce both costs and healthcare usage (Huber et al. 2017).

6.2.2 Cardiac Medication Adherence in Patients with CVD in Australia

In Chapter 3, the results of the cross-sectional survey (Al-Ganmi et al. 2019, Paper revised and submitted to Nursing and Health Sciences) indicated sub-optimal adherence to cardiac medications amongst 37.5% versus 62.5% were adherent of Australian patients with CVD at two stages of the cardiac disease trajectory: prior to admission to hospital and during attendance at out-patient cardiac rehabilitation. Patients attending cardiac rehabilitation reported lower levels of medication adherence (41.9%) than those in an acute care setting (36%). With well over one-third of both sets of patients reporting medium/low adherence, this study's findings are broadly consistent with those of the

World Health Organisation (2003)), which noted rates of non-adherence at around 50%, with differing predictive factors in patients with various chronic diseases including hypertension and CVD. This study's findings are also similar to those of Shah et al. (2009)), who found medication adherence rates ranging from 52% to 66% of patients in cardiac rehabilitation reported medium to high adherence.

Adherence to cardiac medications has been demonstrated to improve through participation in a cardiac rehabilitation program (Desai & Choudhry 2012), but rehabilitation participation rates are low, ranging between 14% and 35% (Kwan & Balady 2012). These results suggest it may be critical to identify the optimal time points at which to deliver interventions to support medication adherence behaviours to overcome individual-related barriers such as inadequate education (Ho et al. 2009), inadequate medication knowledge about disease and medications (Al-Qazaz et al. 2011) and inadequate understanding of the importance of adherence to cardiac medications (Woodruffe et al. 2014). Patients in the early stage of CVD diagnosis, when in-patients of a cardiac ward, are likely to receive intensive monitoring and education (Southard et al. 2003), including on the importance of adherence to medication regimes. However, at this stage medication adherence is a matter of ward routine clinicians may not be aware if patients are likely to experience difficulties with their medications. Cardiac rehabilitation services may not always deliver education in as comprehensive a manner as may occur on the cardiac ward as patients' medication is only one part of rehabilitation and other aspects, such as exercise, may be a stronger focus (Kotseva et al. 2013). This may reflect differences in the organisation of healthcare between cardiac care settings. Other barriers can also pose challenges, including polypharmacy (Grant et al. 2003), beliefs (Park et al. 2018), and practical and attitudinal barriers at the initiation of therapy (Woodruffe et al. 2014). This flags the importance of understanding patients' level of adherence to cardiac medications, particularly after acute phase of illness as the key to improving their self-management and their ultimate outcomes.

6.2.3 Factors Predictive of Medication Adherence in Patients with CVD in Australia

The ability to self-administer and refill cardiac medications, and beliefs about the necessity of medications, concerns about their harm, and fear of overuse of cardiac medications were significant factors in predicting cardiac medication adherence in patients with CVD in Australia. This accords with previous studies showing difficulties of patients in self-administering cardiac medications and refilling them on time. This can be related to the lack of a medication discharge plan, which may then be linked to cardiac complications and recurrent hospitalisation, and may in turn lead to as much as an 80% increase in the odds of premature death (Jackevicius et al. 2008). Similarly, personal beliefs about cardiac medications have been shown to be predictive of adherence in various cardiac diseases (Cicolini et al. 2016, Crawshaw et al. 2016, Foot et al. 2016), suggesting that strategies to address beliefs, including increasing patients' medication knowledge, providing counselling, and using innovative educational methods have the potential to increase medication adherence through improving patients' perceptions and beliefs about medications and their abilities to correctly self-administer and refill their prescribed medications (Unni & Shiyanbola 2016).

6.2.4 Adherence to Cardiac Medications in Patients with CVD in Australia and Iraq

In Chapter 4, the levels of medication adherence and factors potentially predictive of adherence were compared between patients with CVD from Australia and Iraq. This comparative cross-sectional survey conducted in two countries demonstrated that Iraqi patients had significantly lower adherence to cardiac medications than patients from Australia (with 64.3% versus 37.5%, respectively) reported low adherence (Al-Ganmi et al. 2019). Australian cardiac patients in this study reported better adherence than those of other studies, where medication non-adherence rates of between 14% and 43% (McKenzie et al. 2015). However, the level of adherence among Iraqi patients was lower than the World Health Organisation (2003)) global adherence estimate around 50%. These figures suggest that the healthcare system in Iraq, including cardiac disease management, is perhaps in an earlier stage of development than services in Australia, which may explain the lower levels of adherence.

Iraqi patients with CVD may face different barriers than those in other, more economically and structurally developed, countries and this possibility is worthy of investigation. In addition, cultural beliefs about health and disease and beliefs about medications may differ between developed and developing countries. In multicultural societies, such as Australia, these factors may contribute to poor adherence behaviours among people from diverse cultural backgrounds (Alzubaidi et al. 2015). Likewise, cultural differences in understanding of chronic diseases and the role of long-term therapy, differences in access and use of healthcare services, and patient-provider relationships in developed and developing countries may profoundly influence the degree of adherence to medication regimes (Bowry et al. 2011). Differences in religion, including beliefs in fatalism and spirituality, may influence patients' decisions to adhere or not adhere to medication (Dalmida et al. 2017). Beliefs that health, life, and death are in God's hands are prevalent in Middle Eastern countries including Iraq. These beliefs influence attitudes and practices toward disease, and may lead the individuals to take a passive role in their health (Lipson & Meleis 1983).

Cultural norms may explain some differences in personal control and patients' behaviour, and hence may affect self-management in the context of perceived medication adherence (Kucukarslan 2012). Kleinman et al. (2006) claimed that cultural differences may be a contributing factor to medication adherence because individuals' illness perceptions and consequent behaviours such as medication adherence can be influenced by their culture. A cross-sectional study found that differing cultural health perceptions and practices were likely to affect patients' adherence to cardiac medications (Li et al. 2006). For example, lack of trust and concerns about medications among individuals from developing countries may be culturally driven by the low quality of available healthcare services (Griva et al. 2013). Further, cultural beliefs about disease and its management contribute to individuals' adherence to healthcare providers' instructions such as for medication regimes (Shaw et al. 2009). Non-adherence to chronic disease management plans including medication adherence, especially among low-income countries, urban and minority patients, is widespread (Sieben et al. 2019). However, few studies have been conducted on the effect of cultural differences and medication adherence among patients in various settings.

The level of medication adherence rates may also vary according to differences in the healthcare services of resource-limited and resource-rich countries. For example, cardiac rehabilitation programs in western countries emphasise utilisation of the proximity and accessibility of multiple services incorporating home-based exercise programs together with facility-based supervised training sessions to improve health outcomes (Kwan & Balady 2012). These programs do not necessarily translate well to resource-limited countries such as Iraq, where patients can only attend clinic appointments and rely only on their cardiologist or general practitioners for medication counselling and information (Osamor & Owumi 2011). Most patients with cardiac disease in Iraq interact only with their physicians; other healthcare providers seldom communicate with them (Al Hilfi et al. 2013), thereby reducing their support and potentially increasing non-adherence (Bader et al. 2015). These barriers can lead to patients having insufficient knowledge and misperceptions about medications, as they may lack understanding about their medications or they can communicate with provider about experienced side effects.

In the Iraqi cultural context, patients receive support and reminders about taking their medications from their family members and this may reduce patients' likelihood of seeking and interactions with healthcare providers and receiving education and advice. The family structure in Iraq values the necessity of providing care for family members based on cultural and religious beliefs. These values and beliefs may differ to other cultures, such as that of Australia. In addition, given that Iraqi patients were more likely to have lower educational levels and hence health literacy, they may be more likely to err due to misunderstanding any post-discharge instructions, particularly bearing in mind the limitations of the Iraqi healthcare services. Poor rates of non-adherence warrant further investigation. To improve medication adherence in Iraq, individual, cultural, and organisational barriers need to be identified and addressed. Identifying potentially predictive factors for medication adherence can assist in developing and implementing strategies to improve adherence to medication (Jackevicius et al. 2008).

6.2.5 Factors Potentially Predictive of Medication Adherence in Patients with CVD in Australia and Iraq

In Chapter 4, the findings of the survey, conducted in both Australia and Iraq revealed that the ability to correctly self-administer and refill medications, and beliefs about cardio-protective medications were independent predictors of cardiac medication adherence behaviour in both Australian and Iraqi patients with CVD. These findings are consistent with the results of previous studies with other patient groups, such as patients with hypertension (Zeller et al. 2008) and patients with CVD (Reidel et al. 2008), where the ability to refill medication independently predicted adherence behaviour; however the association declined with increasing regime complexity. These findings also are congruent with those of Ruppar et al. (2012) who found that stronger belief in the necessity of antihypertensive medications could predict better adherence. Similarly, in patients with negative beliefs about the necessity of their medications, non-adherence rates were double that of those with less negative beliefs (Gatti et al. 2009). These patients were more likely to intentionally skip doses and report forgetfulness (World Health Organisation 2003). Similar findings have been reported in studies conducted in Oman, where stronger beliefs about the necessity of hypertensive medications were significant predictors of medication adherence (Al-Noumani et al. 2017). This suggests that major behavioural drivers may be similar across countries, or operate through similar mechanisms despite cultural, religious, resource and infrastructure differences. Previous studies have suggested that patients' ability to self-administer and refill medications, and their beliefs about medications, may be affected by patient-related determinants such as level of education (Park et al. 2015), the number of medications they are prescribed (Karakurt & Kaşikçi 2012) and their comorbid conditions (Molloy & O'Carroll 2017). Given the differing contexts, and the variations in the sociodemographic characteristics of the Australian and Iraqi groups, differing effects might have been anticipated in relation to patients' ability to self-administer and refill medications, and their beliefs about medications.

In Iraq, the location of recruitment (cardiac ward versus cardiac clinics) was significantly predictive of medication adherence, with patients recruited from out-patient cardiac clinics significantly more likely to report higher adherence than patients recruited from a cardiac ward. The overall lower adherence rate in Iraqi patients may be attributed to the quality of CVD services regarding medication counselling and education delivered in in-patient and out-patient settings. Perhaps patients attending clinics may be generally more motivated, perseverant, and willing to attend follow-up with their cardiologists, with consequently relatively better medication adherence (Bedell et al. 2000). It is also possible that patients attending cardiac clinics may have had more opportunities to receive more education and counselling regarding their medications. This in line with a previous study by Morisky et al. (2008)), which indicated that patients who visit out-patient settings are provided education regarding chronic disease care, and their misunderstandings regarding cardiac prescribed regimes are corrected reducing stress; they also learn about improving coping skills, and establishing treatment regimes to improve medication adherence.

A comprehensive discharge plan, including instruction by nurses and pharmacists, and counselling pre-and post-hospital discharge may improve patients' understanding of their medications (Verloo et al. 2017). A broader understanding of patients' goals and strategies may enable a focus on patients' adherence beliefs and behaviours, and establishment of organisational policies and procedures to take advantage of these. To achieve this, cultural differences between patient groups should be further studied so their effects can be better understood and considered. Patients' cultures, social settings, and cardiac journey at the point of study should all be taken into account and targeted with nurse-led education interventions designed to address patients' beliefs about their medications and their ability to self-administer and refill them. Medication counselling and education at discharge provided by nurses has been associated with improved ability to refill medication, medication knowledge and adherence (Jackevicius et al. 2008), and more reasonable beliefs about their medications (Farmer et al. 2012).

6.3 Adherence to Cardiac Medications

The prevalence rates of medication non-adherence vary across settings and countries in adult patients with various chronic diseases, but these reported discrepancies may be as much due to methodological differences as true variation in rates (Andrade et al. 2006). Using a cross-sectional survey design, these findings demonstrated that adherence to cardiac medication was lower among patients in Australia to those in Iraq. In this study, individual-related factors and health related-factors were not significantly predictive of medication adherence in either country. However, in some other studies these individual-related factors have been identified as key predictors of medication non-adherence (Novick et al. 2010), supporting the potential impact of sociodemographic characteristics on medication adherence (Kang et al. 2015).

Patients attending cardiac rehabilitation and out-patient cardiac clinics were more likely to be members of the younger elderly age group (≤64 years) than those admitted to cardiac wards in Australia and Iraq, although this was not statistically significant. Several studies have reported younger age is more often predictive of poor adherence to cardiac medications (Hadi & Rostami 2004, Lee et al. 2013, Wang et al. 2014, Yang et al. 2016). Potential mechanisms linking younger age and non-adherence to cardio-protective medications include lower motivation on the part of patients with less severe diseases, less interest in the assistance with medication use provided by caregivers and believing that the severity of cardiac disease can be reduced by exercise or weight loss (Monanae et al. 1996). Lower adherence among younger patients may also be a consequence of lesser contact with healthcare professionals, and perhaps of their perception that they receive no immediate benefit from their medication. Identifying younger patients with non-adherence behaviours is important as they are at increased risk of rehospitalisation; it may be appropriate to target these patients to ensure that they have a clear understanding of the importance of taking their medications regularly. However, other studies have found that younger patients have higher medication adherence (Wei et al. 2004, Ibrahim et al. 2011, Valeria et al. 2011, Zhu et al. 2011, Sanfélix-Gimeno et al. 2013). Among younger patients, a possible explanation may be their relatively lower number of comorbidities, and their perceptions of themselves as healthier.

Older patients have also been reported as more likely to better adhere to their medication regimes (Harper et al. 2018). Previous studies suggested that elderly patients are more likely to be adherent due to their more frequent contact with healthcare professionals; further, a proportion will be in supervised care with strict routines for administering medication, particularly if they have previous hospital admissions for recurrent cardiac events (Newby et al. 2006). Older patients are more likely to have concomitant presence of more comorbidities, leading to their perception of themselves as being sicker, which may cause them to ensure they take their medication (Wang et al. 2014). Clearly, the association between age and adherence to medication can vary across the age continuum, and conclusions in relation to this tend to be mixed in the literature. Collectively, age-related barriers have been shown to influence the ability and willingness of both younger and older adults to take their medications. Most cardiac patients in this study were older, and the findings indicate that researchers should seek to improve adherence cardiac medications in these age groups as well as amongst younger patients. It is therefore possible that any apparent relation between adherence and age may be mediated by other factors.

This study found that Australian patients had a higher level of education than patients from Iraq. In Australia patients attending cardiac rehabilitation were better educated and yet showed low adherence, while Iraqi patients attending out-patient cardiac clinics were less educated and also had low adherence. Poor adherence to medication may be predicted by lower levels of education (Wang et al. 2014); Iraqi patients with lower levels of education may not strictly follow the medication regime prescribed by their doctors as they may be uncertain, and perceive conflicts of opinion where they misunderstand and therefore fail to adhere to their medications. Other possible reasons may include lower health literacy levels, which has often been reported as more common among elderly and minority people because they are likely to be less well educated and experience language barriers, which are also obstacles to medication adherence (Vlasnik et al. 2005).

Studies have demonstrated mixed and conflicting findings on the effect of health literacy on adherence to medications (Zhang et al. 2014). Patients who lack health literacy may find difficulty following medication instructions, contributing to poor medication adherence; this has been considered a highly challenging factor to address (Minn 2009). Karakurt & Kaşikçi (2012) have argued that patients with only primary education or who are illiterate fail to adhere to their medications because they are unable to understand the importance of engaging in positive health behaviours or to develop a coherent understanding of their importance despite the efforts of healthcare providers to explain this. The quality of the provider-patient relationship may also be an important determinant, with a critical factor being a patient's respect, faith or belief in their physician and what they tell them (Eagle et al. 2004).

Surprisingly, Australian patients who attended cardiac rehabilitation sessions were significantly better educated but also less adherent to their medication. Overall, patients with more years of education tend to have better health and health behaviours (Lindquist et al. 2012); however, this was not found among this Australian cohort. A possible explanation is that highly educated patients may not always follow the healthcare instructions provided by cardiologists and pharmacists if they interfere with their busy life style (Awad et al. 2017). This finding highlights the need for further in-depth qualitative studies to provide better understanding of education as a possible factor for non-adherence among patients with CVD in both Australia and Iraq. Overall, Iraqi patients had lower levels of education than those in Australia and they may have less opportunities to attend cardiac clinics, which influences their attitude and may be related to their lower level of medication adherence. However, it appears that both Iraqi and Australian patients need additional education regarding the importance of medication adherence, and effective communication with their healthcare providers to improve their medication adherence.

This study indicated that patients attending for cardiac follow-up (cardiac rehabilitation in Australia or out-patient cardiac clinics in Iraq) were more likely to be married or co-habiting (Al-Ganmi et al. 2019). Married patients or those living with family members have been reported with better adherence to medication, perhaps because they have someone to remind them to take their medication (Wu et al. 2008). The impact on adherence of being married or in a relationship suggests that a partner who reinforces or reminds a cardiac patient is providing practical support for their treatment regime or is perhaps reinforcing the patient's self-management. Studies have found that unmarried patients are more likely to be non-adherent and twice as likely to experience cardiac events than married patients (Wu et al. 2012). However, in this study, patients with partners were more likely to report non-adherence, possibly because they had low family support or low motivation. This was particularly true of Iraqi patients, who may have had additional problems such as limited access to medications or lesser ability to afford regular medication. This is consistent with the findings of Bader et al. (2015), that non-adherence may be attributed to the financial burden of family. Another possible explanation is that the quality of the relationship between partners may influence secondary prevention behaviours such as adherence to medication (Molloy et al. 2008) where benefits may accrue for adherence to medication from being married. However, marital status may also have various negative effects for patients, such as distress, depression, and anxiety, depending on how the partner shares the emotional burden and provides support. Practical support is a potentially important target and developing interventions in this area may reduce healthcare costs and improve adherence. This study highlights the importance of the role of social structures such as marital status and the financial burden of medications (Marcum et al. 2013), which are often underrepresented as predictors of adherence in CVD and thus require further study.

For neither Australian nor Iraqi patients was employment status significantly predictive of medication adherence. However, Australian non-adherent patients undergoing cardiac rehabilitation were more likely to be employed, while the Iraqi patients recruited from out-patient cardiac clinics were more likely to be unemployed. Employed patients who attended cardiac rehabilitation in Australia tended to be less adherent to their cardiac medications than unemployed or retired patients. This finding is consistent with the findings of Kang et al. (2015). A reasonable explanation may be that employed patients may experience time demands and instability in their daily routine, such as irregular shift work, which may contribute to skipping doses. Such patients may be occupied with work duties that have the potential to disturb a medication schedule, and they may not be able to maintain a regular habit of medication adherence and may also have little time for self-care or management (Obirikorang et al. 2018).

On the other hand, of the patients recruited from out-patient cardiac clinics in Iraq, those who were unemployed were more likely to be non-adherent than those who were employed. Some studies have shown that unemployed patients tend to have poorer adherence (Kassab et al. 2013); and for these patients, particularly, the lack of healthcare coverage is a hidden issue that is now emerging (Lee et al. 2013). It is possible that the association between unemployment and poor adherence may be mediated by the provision of low-cost subsidies; however, this form of medical service is relatively inaccessible in Iraq. The differences between the effect of employment status in Australia and Iraq may be a factor of the differences in the healthcare systems and practices of each country. It may also be a result of cultural differences in work patterns in Iraq. It is a challenge in this study to make a clear connection between those adhering to a prescribed medication regime and their commitment to a daily work routine. This is perhaps due in part to the inconsistent nature and the structure of employment, whether full-time or part-time; whether regularly scheduled or shift work. For example, the Iraqi attitude towards work and lifestyle do not generally favour the fixed job routines that are common in other cultures, and among Western populations (Virtanen et al. 2002), and therefore it cannot be assumed that employment status has the same impact in each country in this study.

Patients with comorbidities may have greater risks of non-adherence for many possible reasons. This study did not find the presence of comorbidities, particularly diabetes mellitus, a significant predictor of medication adherence among patients in Australia or Iraq. Patients from Iraq were more likely to have comorbidities than patients from Australia. The Iraqi patients with CVD also had lower adherence to medication than those from Australia. Patients with more comorbidities might perceive themselves as more sick and helpless, and if this is exacerbated by absent-mindedness (perhaps related to the minor cognitive impairment that is commonly associated with long-term CVD or diabetes) (Vincent et al. 2014), or by poor family or social support, it may be linked to poor medication adherence. Perhaps their involvement with the healthcare system is more intense and they have more cardiac medications. Patients with increasing numbers of comorbidities and multi-morbidity need to manage more complex regimes for multiple conditions (Stack et al. 2008). A lack of understanding of medications and disease may play a role in patients' adherence and self-management difficulties. Patients from Iraq were less likely to adhere to medication; this may be attributed to complications that they develop due to poor disease control. Another study (Wong et al. 2014) showed that the prevalence of non-adherence increased among patients with a larger number of comorbidities, and that they were more likely to perceive their health condition as poor. Patients with multiple chronic diseases may regard some medications as being more important and undervalue the significance of others. Iraqi patients with comorbidities may encounter difficulties in complying with a medication schedule if they have poor bodily functions and must deal with multiple medications and their various side-effects.

Iraqi patients with multiple conditions may perhaps be overwhelmed by apparently conflicting instructions, a result of fragmented care within a complex health system. In addition, patient education in out-patient cardiac clinics in Iraq may be inadequate for patients with chronic illnesses including CVD. Thus, medication adherence among patients with comorbidities may differ to that of patients solely with CVD because of the differences in knowledge about each disease and treatment, their satisfaction with treatment, the sophistication of their treatment services and the effectiveness of their patient–clinician interactions, and their ability to adhere to more complex drug therapy routines.

Cultural considerations may underpin a wide range of diverse influences on medication adherence, but cultural homogeneity should not be assumed within nations or national groups. Although Iraqis generally are a religious and conservative people, there are also strong secular tendencies in the country (Alwan 2013). Iraq is a Muslim nation and considered a collectivistic society. This is manifest in a close long-term commitment to the member 'group', be that a family, extended family, or extended relationships. Loyalty in a collectivist culture is paramount, and over-rides most other societal rules and regulations. Arab Middle Eastern cultures such as Iraq tend to use more of an integrating and avoiding style in handling interpersonal conflict (Al Hilfi et al. 2013).

Australia is widely recognised as a diverse multicultural country; people come from nearly 200 countries and represent more than 300 ethnic ancestries, with one in four people in Australia (26%) born overseas (Australian Bureau of Statistics 2016). Australian culture is generally categorised as individualistic in nature (Gudykunst et al. 1996). In Australia, individuals have the right to a private life and to take care of themselves. They are self-oriented and emotionally independent, and their emphasis is generally on individual initiative, the right to privacy, autonomy, and individual decisions (Bond & Forgas 1984). The Australian cultural identity is based in their social system, and a wide variety of social groups, institutes and organisations. The Australian culture tend to use more of an obliging, dominating and compromising style in handling interpersonal conflict (Heinke & Louis 2009). Hence, there are distinct differences between and within Australian and Iraqi cultures.

The healthcare systems of both countries have to be able to respond appropriately to a degree of cultural diversity. For Australia, there is a high degree of diversity, and hence there are lessons to be learned from Iraq about how people in a very different cultural context respond to medication regimes. For Iraq, as a country where there is a degree of secularity within an otherwise predominantly religious culture, there are lessons to be learned about the influential factors at play in secular societies. Hence, medication adherence interventions can address the specific needs of individual cultural groups to improve adherence and outcomes among patients who are racially, religiously and ethnically diverse. In both countries, interventions to enhance medication adherence may be accompanied by applying cultural competence strategies via healthcare providers who should be able to understand and integrate cultural intelligence into the delivery of healthcare. Culturally competent healthcare services may provide patients with a consistent quality of care, regardless of their cultural, religious, racial, or background. It is crucial for healthcare providers such as nurses to identify patients' religious and spiritual beliefs and needs and provide an opportunity to discuss these to tailor medication intervention and meet patients' specific needs. The process of developing culturally-related interventions from patient perspectives can assist in promoting strategies that might normally not conceptualised if they were developed from health professionals' perspectives.

Patients from Iraq were more likely to take a higher number of cardiac medications than patients from Australia. The complexity of taking many medications at different times a day with the right amount of medication on schedule may contribute to low adherence, particularly if they must follow complicated routines. The quantity and size of pills may make it difficult for patients to take all their medications, which may also limit their adherence (Borgsteede et al. 2011). In this study there was some suggestion of intentional non-adherence among Iraqi multi-morbid patients with polypharmacy, who may find that taking multiple medications leads to unexpected and unpleasant side effects. This may lead them to consider the benefits of taking all their medications, and lead to non-adherence. This indicates the importance of keeping patients' medication regimes to a minimum and particularly the daily dose frequencies for patients with comorbidities (Ramli et al. 2012), also taking into consideration medication-related costs (Dennis et al. 2011). The problem of non-adherence among patients with multiple chronic diseases may be overcome, at least in part, by optimising the number of medications and simplifying dose schedules. There is a role for nursing in this; the clinical nurse at every point in the cardiac trajectory should focus on patient self-management and work closely with other healthcare providers such as general practitioners, cardiologists and pharmacists.

In clinical practice generally, there is little understanding or account taken of how patient-specific sociodemographic and health-related factors influence medication adherence, and how effective interventions can be targeted to overcome barriers and improve adherence in patients with CVD. Understanding patient-specific factors is crucial to ensure that organisational level interventions are designed to meet patient needs; to understand patients' perspectives of how healthcare systems facilitate or hinder medication adherence.

With the increasing prevalence of CVD in Australia and Iraq, it is crucial to identify the prevalence rates of non-adherence among this critical population to promote secondary preventive approaches to improve health outcomes. However, data from Australia and Middle Eastern countries are scant, prompting this study. It is widely known that there are major gaps in socio-economic development and health disparities between developed and developing countries (Pereira et al. 2009). When these data were collected, the Iraqi health system was struggling to recover from years of war and shortages and was seeing the emergence of an expensive private health sector (The Iraqi Ministry of Health 2012). Iraqi patients with CVD might have experienced particular issues in accessing quality health services due to the lack or limitation of resources for specific clinical services, including the provision of medications in public hospitals (Al Hilfi et al. 2013) or in the community. However, this was not the case for the Australian sample, where common cardiac medications are provided through a system of public subsidy. Poor rates of non-adherence warrant investigation to identify potential predictive factors and implement strategies to improve adherence to cardiac medications across differing contexts and environments.

Variations in non-adherence characteristics among cardiac patients from developed and developing countries makes comparisons across studies and across cardiovascular conditions difficult (Ho et al. 2009). This flags the importance of researchers investigating factors influencing non-adherence to cardiovascular medications in patients with CVD in routine clinical practice, to optimise health outcomes. The high prevalence of non-adherence to cardioprotective medications in both developed and developing countries such as Australia and Iraq makes it imperative to understand the factors that influence adherence behaviours to cardiac medications to understand longitudinal changes in adherence, the impact of non-adherence on physiological measures, and the development of tailored nurse-led interventions capable of overcoming patient-specific sociodemographic and health-related determinants of non-adherence.

6.4 Significant Predictors of Non-adherence to Cardiac Medications

In this study, patients' attitudes and behaviours that predicted medication adherence and may therefore mediate relationships between treatment and outcomes included the ability to self-administer and to refill medication, and beliefs about medication. The ability to correctly self-administer and refill medications significantly predicted adherence to cardio-protective medications in both Australia and Iraq (Al-Ganmi et al. 2019); Al-Ganmi et al. 2019, Paper revised and submitted to Nursing and Health Science). For patients with CVD from various settings and across countries these factors predicted medication adherence behaviours, regardless of differing sociocultural and economic contexts.

6.4.1 Attitudes in Relation to the Theory of Planned Behaviour: Beliefs about Cardio-protective Medication

Medication adherence or non-adherence is directly linked to an individual's specific and general beliefs about whether the medications have beneficial or detrimental effects for their health (Cicolini et al. 2016). Patients with chronic diseases such as CVD experience a variety of symptoms and are likely to be prescribed a significant number of medications, which makes it difficult to assess their beliefs about a specific medication or diseases (Holmes et al. 2014). Adherence may be influenced by beliefs about medication, as when a patient decides to take medications in a different way from that described by the provider; in such cases non-adherence is neither accidental nor random, but a result of the patient's intentional decision (Foot et al. 2016). Beliefs about medication may offer greater predictability than other clinical or social factors (Horne & Weinman 1999). Strong beliefs in the necessity of medication and few concerns about the adverse effects of medication predict medication adherence (Crawshaw et al. 2016).

According to Theory of Planned Behaviour (TPB) (Ajzen 1991), individuals' beliefs are strong predictors of behavioural intentions and possibly of actual health behaviours such as medication adherence. The findings of this study highlighted that Australian and Iraqi patients shared similar beliefs about the necessity (or otherwise) of taking cardiac medications (Al-Ganmi et al. 2019): findings that provide further support to the Theory of Planned Behaviour (TPB). This study findings are in line with the TPB proposition that medication adherence intention can be influenced by patient attitudes toward adherence behaviour, which can be determined by their beliefs about the necessity of performing this behaviour (Redding et al. 2000). Park et al. (2018) found that patients with high need for medications, high beliefs about the necessity of medications and low concern had higher adherence. Patients often have concerns about drug dependence or medication side effects (Mukhtar et al. 2014). Patients should be supported to develop strong beliefs about necessity of their medications, which can contribute substantially to positive medication adherence.

For those patients with increased levels of concern about using medications, this contributed to poor adherence. This may imply that patients did not perceive the management benefits, only their susceptibility to the disease related complications. Beliefs in the necessity of taking medications may reflect patients' awareness of their illness and the importance of the medications for treating their illness. Hence, this can influence patients' motivations to take their medications. A patient-oriented approach by healthcare providers such as clinical nurses may help maintain positive beliefs about the necessity of medications. Enriching patients' knowledge about their diseases and prescribed medications may help them understand their medications as a necessity, while their lack of knowledge may result in concerns about taking their medications. Survey findings showed that patients with CVD from Australia and Iraq held similar adherence behaviours despite the socio-eco-cultural differences and beliefs about the necessity of medication was consistently a predictive factor of adherence, flagging this predictor as an important factor affecting medication adherence across cultures.

Beliefs about medication convenience and higher number of prescribed medications and regime complexity have been reported as predictors of non-adherence (de Vries et al. 2014). The study findings also indicated that Australian patients had general beliefs about overuse of medications: that their physicians prescribed too many. Patients may have negative views about medications (addiction or overuse, long-term side-effects), and about medication over-prescription by their physicians (Horne et al. 2013). Patients with polypharmacy may deny having serious disease and translate this into general beliefs about medication overuse. It is possible that patients on more medications may be more likely to adhere because of greater disease severity concern, or knowledge, or a more established regime. This study found beliefs about overuse of medication, suggesting lower adherence by patients with complex regimes due to patients' concerns about medication. This suggests that patients may have poor communication with their doctors in term of explaining the necessity of medication, which may affect their medication adherence.

Patients may be more likely to forget taking medication, if they have more negative attitudes toward medication in general and therefore, perhaps medication overuse beliefs affect unintentional non-adherence. Accordingly, patients with positive attitudes towards health are more likely to better remember health-related information (Barat et al. 2001). Patients with CVD often have comorbidity and are likely to be prescribed with multiple medications, where this occurs, concerns about medication overuse. Therefore, those patients may benefit from early assessment of their beliefs about medication to prevent further risk of developing other complications related to suboptimal adherence to medication. In the long term such intervention may reduce the financial burden on the healthcare systems by reducing the costs of treating complications related to suboptimal adherence. Nurses and other healthcare providers should understand and shape the dimensions of the provider-patient relationship in relation to communication processes, patients' engagement in their management plans and sustaining longer term relationships.

In the current study, beliefs about the general harm of medications was a significant predictor among cardiac patients from Iraq. Beliefs about general harm contributes to a general feeling of mistrust in medication (Schüz et al. 2011). This suggests that unintentional non-adherence may be predicted by changes in general beliefs about harm of medications; if patients have a belief that their medications will have adverse effects on their health and complications, they are more likely to intentionally or unintentionally avoid taking their medications. Similarly, if patients experienced medication adverse effects and they did not have opportunities to be counselled by doctors or other healthcare professionals, they may be more likely to not take their medications. Within an unsustainable healthcare system such as in Iraq, and with relatively poor economic status, it is difficult for patients with CVD to have opportunity to be advised about their medication problems. Patients may have to depend on themselves if they need knowledge about their medications. This is especially a concern if they have low educational level and health literacy. Healthcare professionals, especially nurses, should provide patients with adequate information about medications and answer patients' questions about the possible harms of those medications.

6.4.2 Behaviours in Relation to the TPB: Self-administration and Ability to Refill Medication

Medication non-adherence is compounded by difficulties in determining how patients use their medications, and suboptimal adherence to regimes is multifactorial. With advanced age, many patients will have reduced vision, hearing and dexterity, which may make it difficult to for example, deal with complex prescribed medication regimes, read prescription labels, and discriminate tablet shapes and colours (Russell et al. 2006). Patients' ability to refill their medication depends on their attitudes and other individual and health-related factors such as disease characteristics and the type of medication being used (Krigsman et al. 2007). Medication self-management ability allows patients to recognise any problems related to their medication, and provides techniques to help them make decisions, plan appropriate actions, and take and change these actions in response to changes in their medication circumstances or disease. This study showed a strong link between the ability to self-administer and refill medications and medication adherence, a finding that is likely to be applicable internationally.

Ajzen's Theory of Planned Behaviour (TPB) (Ajzen 1991) posits that three key elements (attitude, subjective norms, and perceived behavioural control) predict a person's intent to engage in a behaviour such as medication adherence, and behavioural intention, in turn, predicts behaviour. The patient's behavioural intention to take medication might be influenced by factors which may be beyond an individual's control, including ability to self-administer and refill medications and their psychosocial and health characteristics (Crawshaw 2016). Elements of the Theory of Planned Behaviour were shown to help define the ability to refill cardiac medication as attitudes and behaviours that predict greater medication adherence and mediate the relationship between treatment and medication adherence (Lin et al. 2016). In this study, patients who were more likely to form intentions about non-adherence to recommended medications were more likely to have negative attitudes resulting in failure to self-administer and refill their medications due to carelessness, perceived medication side effects, perceived high risk and low benefits. According to the TPB, the likelihood of weak behavioural intention, and subsequently action, increases with more negative attitudes. To the extent that attitudes reflects intention and actual behaviour, attitudes contribute directly to the prediction of medication adherence.

In both Australia and Iraq, with data analysed in combination or individually for each country, the ability to correctly self-administer and refill medications independently predicted adherence behaviours. Iraqi patients were shown to be more likely to stop taking their cardiac medication intentionally, indicating low medication self-management based on the ability to refill their medications and suggesting a possible link with socio-economic, demographic and health-related factors (Al-Ganmi et al. 2019). Various patient-related determinants of the decision to adhere to medication have been identified in the literature, both as intentional and nonintentional factors (Ho et al. 2009). Patients may stop taking medication intentionally if the medications are felt to be ineffective, unsafe, unnecessary or costly (Atinga et al. 2018). Patients may not adhere to cardiac medications if they have experienced unpleasant side effects, outweighing their perceptions of the benefits of the medication. Patients may feel better after stopping their medications, misunderstanding the concept of a therapeutic dose. Patients may perceive a high risk if they take medications whilst they perceive low benefit because of their disease complications and they feel well without taking medications (Youssef & Moubarak 2002).

In developed countries such as Australia where the health system offers support through Medicare benefits, patients are better able to afford their medications which are provided at relatively lower cost. Despite this, this study found that Australian patients intentionally stopped refilling their medication, citing high costs. A qualitative study of Australian community settings reported a high prevalence of intentional non-adherence among patients with chronic diseases (Laba et al. 2015). This suggests that elderly and retired or unemployed people in Australia may find it difficult to afford their medications even when they are heavily subsidised, especially if they struggle to meet the basic cost of everyday living. A formal analysis of direct and indirect costs would be an essential part of future studies, providing preliminary data about unforeseen medication cost-related barriers to medication adherence. Possible facilitators to overcome medication cost and non-adherence may include seeking the support of local and national medication scheme administrators and raising clinicians' awareness of the problem of medication costs. The roles of clinical nurse and nurse manager at the point of care in cardiac services can be instrumental in coordinating care and support for patients' medication self-management abilities and discussing specific strategies to manage medical costs. The clinical nurse should also provide practical information about how to fit medications into daily routines, and this can support patients in their adherence to medication.

6.4.3 Organisational Influenced on Adherence Behaviours

Many health-related behaviours are largely dependent on individuals' attitudes, yet intention in clinical behaviours may also be affected by factors such as access to, or the quality of services or availability of resources (Godin & Kok 1996). The ability to refill medications may also be explained by the quality of the patient-clinician relationship. It has been reported that a mistrusting and non-supportive relationship between patients and their clinicians increases inability to self-administer, reduces medication refills and increases non-adherence (Krueger et al. 2005). This is an organisation-related concern, as the patient-healthcare provider relationship and the clinical setting routine have been predictive of non-adherence for patients with CVD (Brown & Bussell 2011). A previous study has shown the influence of a poor therapeutic relationship between a patient and healthcare provider, and lack of communication, where this can be associated with a lack of confidence in healthcare providers (Alzubaidi et al. 2015). This relationship may link to the issue of patient support by the health system through medication education and counselling, and hospital regulations requiring continuity of care (Hesselink et al. 2014). Poor patient-provider communication may link to the patients' low literacy, which may also be a barrier to communication with healthcare providers. Previous studies have demonstrated that patients with limited English proficiency have limited access to healthcare services and perceive a lower healthcare quality (Krueger et al. 2005). Effective patient-provider support is an important component of delivering quality healthcare such as promoting increased adherence to medications (Li et al. 2017).

An effective and collegial physician-patient interaction is necessary to change patients' misconceptions about medication use (Eagle et al. 2004). The principle of concordance between patients and healthcare professionals is a crucial aspect of the relationship; requiring participatory approach (McCann et al. 2008). Asking patients about their difficulties in taking their cardiac medications and following up closely, may be effective as part of routine practice, and may help to reduce failure to medicate (Brookhart et al. 2007). Providers such as physicians, pharmacists and nurses should provide a structured and extended discussion with patients about their medications and ascertain whether they understand, for example, by asking the patient to repeat what they have been instructed (Makaryus & Friedman 2005).

Despite the significant association for both Australian and Iraqi groups of the ability to correctly self-administer and refill medications and adherence behaviours, the study findings showed differences in the suboptimal adherence rates in both groups (Al-Ganmi et al. 2019). The TPB indicates that behavioural intentions mediate the relationship between behaviour relevant beliefs and behavioural engagement. The TPB posits that extent to which favourable behavioural intentions are translated into actual behaviour may be moderated by the extent to which an individual has control over engaging in the behaviour. Patients may be unable to correctly self-administer and refill their medication for a number of physical, cognitive, sociocultural and economic reasons. In Iraq, patients may be more vulnerable to unintentional non-adherence, and may struggle to achieve medication self-management if they have had little education, have low health literacy, suffer from more comorbid diseases or take a larger number of cardiac medications (Al-Ganmi et al. 2019). Intentional non-adherence may also derive from educational and motivational determinants that influence patients' behaviour (Schüz et al. 2011). The identification of differences in the patients' ability in medication self-management between different cultural groups suggests the need for greater understanding of the effect of cultural background on medication use with potential implications for the conduct of medication consultations and provision of patient knowledge on medication. This is not just an issue for other countries; since Australia is a multi-cultural country, it is important that healthcare providers, including nurses, are able to understand the impact of cultural background on the ability to self-administer and refill medications and how this knowledge might be used to improve healthcare delivery at all points of cardiac care settings (Horne et al. 2004).

6.5 Proposal for Nurse-Led Interventions to Improve Medication Adherence

In Chapter 5, a proposal was presented (Al-Ganmi et al. 2018), designed as a pilot RCT suitable for testing the effectiveness of an evidence-based, nurse-led intervention to promote medication adherence in patients with CVD, informed by findings and recommendations of the systematic review of medication adherence interventions (Al‐Ganmi et al. 2016) and taking account of the survey findings ((Al-Ganmi et al. 2019); Al-Ganmi et al. 2019, Paper revised and submitted to Nursing and Health Science). This proposal recognises the evidence that multi-faceted medication adherence interventions, comprising components such as motivational interviewing and text message reminders, may improve adherence to cardiac medication regimes by targeting individual non-adherence behaviours.

In this proposal, the level of adherence to cardiovascular medications will be assessed in patients referred to a cardiac rehabilitation program or cardiac clinic follow-up after hospital admission for an acute cardiac event and to the feasibility and effectiveness a multi-faceted intervention will be tested. The role of individual, behavioural and environmental factors in predicting non-adherence will be examined. This will include a focus on the ability to self-administer and refill medications, and beliefs about cardiac medication regimes, taking into account individual and local situations and contexts, including, for example, the geo-political situation of the Middle East (in the case of Iraq). In developed nations like Australia, this will have implications for future behavioural interventions delivered by nurses to improve medication adherence, taking into account the cultural background of patients in these countries.

A multifaceted intervention comprising motivational interviewing counselling plus other interventions such as text message reminders may have a significant influence on patient adherence to their cardiac medication regimes (Al-Ganmi et al. 2018). Motivational interviewing intervention studies have reported effecting significant changes in adherence behaviour in patients with CVD (Faulkner et al. 2000, Ogedegbe et al. 2008, Ma et al. 2014) and to improve adherence to medications when delivered by nurses (DiIorio et al. 2008). Motivational interviewing can be delivered in different modes such as face-to-face counselling and phone-based interviews (Palacio et al. 2016), and nurses who use this technique should intentionally influence and resolve patients' ambivalence to change to elicit intrinsic motivation to enable behavioural change (Dobber et al. 2018).

Studies have shown that nurses can be effective at improving adherence among patients with CVD (Konkle-Parker 2001). Nurses are uniquely positioned to provide motivational interviewing counselling to improve medication adherence and overall health outcomes. This includes counselling patients about their cardiac medications, monitoring medication use, and communicating with other health care professionals

(Jansink et al. 2009). The success of motivational interviewing for medication adherence in patients with CVD can be linked to the use of the identified predictive factors and to knowledge and use of the patients' socio-eco-cultural characteristics.

To adapt the intervention to be appropriate to the needs of patients with CVD from Iraq, a culturally tailored medication adherence intervention including motivational interviewing counselling and text messaging reminders can be developed based on the level of medication adherence and factors that hinder their adherence. The contents of the culturally tailored interventions (e.g. family group meeting) can be contextually grounded in the Iraqi culture and challenges that interventionist face, being tailored towards patient-centred educational approaches that allow them to explore the individual beliefs underpinning medication adherence (Saha et al. 2008). Motivational interviewing counselling for Iraqi patients with CVD can be structured as 30-minutes culturally appropriate counselling sessions during hospital stay, including discussion about the patient's beliefs in the necessity of and perceptions about medications prescribed by healthcare professionals. This can be repeated at 2-week intervals after medication adherence assessment. Culturally tailored text message reminders can be designed to take one minute (no more than 100 characters) to read. Iraqi patients can receive daily culturally tailored text messages reminders via their phones for the duration of the intervention period. Daily text message reminders can be easy to access and checked by the Iraqi patients. The intervention is expected to lead to significant improvement in cardiac medication adherence among patients from Iraq. Culturally tailored medication adherence interventions have the capacity to provide patients with specific strategies to improve adherence to their medications and reduce the effect of factors that influence adherence, including potential individual, behavioural and environmental factors (Conn et al. 2014). These strategies could boost patients' confidence to address medication adherence problems and improve their overall cardiac health. The usage and satisfaction with culturally tailored interventions including motivational interviewing counselling and text message reminders, including the content and customisation, can be assessed through interviewing patients face to face or by text messaging or email. The process of developing interventions for Australian patients with CVD can be similar to that for development of intervention for Iraqi patients but addressing the intervention to the Australian culture.

The combination of a successful approach as motivational interviewing with another technique such as text message reminder or phone call counselling has shown promising results in improving medication adherence among patients with CVD (Al‐Ganmi et al. 2016). Text message reminders are scalable and cost-effective behaviour-change interventions, capable of improving adherence to cardiac medications by increasing patients' intentions towards medication persistency (Adler et al. 2017). Text messaging has enabled healthcare providers to transmit health information to patients and engage them in brief conversations (Nglazi et al. 2013). Studies have demonstrated that text message reminders improved clinical outcomes, physical activity, and psychosocial outcomes among patients with cardiac disease attending cardiac rehabilitation programs (Munro et al. 2013). Mobile phones are becoming an important way of encouraging better nurse-patient communication and may increase in application over the coming years (Mitra et al. 2012).

The most effective interventions to improve medication adherence and clinical outcomes have been shown to be complex, multi-component and intensive, but few studies have been designed to allow exploration of the reasons for success or failure of interventions and their delivery. It is important that healthcare professionals are aware of the effective practical interventions and strategies and are up skilled to deliver them in various healthcare settings. Effectively countering non-adherence behaviour demands multiple efforts in collaboration with various healthcare providers in order to tackle the many barriers to successful adherence. Nurses currently represent an underestimated and underutilised force in improving adherence and care outcomes (World Health Organisation 2003). This study findings highlight and support the successful role of nurses in adherence care (Al‐Ganmi et al. 2016). Their presence in all health care settings, their closeness to patients and their large numbers may position them for sustained adherence enhancing strategies (Van Camp et al. 2013). To be successful, nurses need to understand the personal, behavioural and environmental factors predictive of a patient's adherence to medication regimes. For example, in the , cardiac are indicated for patients with cardiac impairments that result from a wide range of cardiac pathologies and the majority of patients who present with cardiac impairments or diagnosis receive at least one or more cardiac medication. These patients may simultaneously experience significant change in their ability to engage in daily activities due to cognitive impairment and loss of motor skills (Collins & Dias 2013), which may impact on their ability to learn, including in relation to their medication regime. Given the prevalence of cardiac disease complications with multiple prescribed medications, many such patients may struggle to learn what they need to know to support their ongoing adherence to their medications in the acute care setting, particularly. Healthcare professionals including cardiac nurses should take into consideration the patients' ability to engage in behaviour change and educational interventions for medication adherence (Verloo et al. 2017).

6.6 Strengths and Limitations of the Study

Based on the published and under review research findings, this study is among the first to investigate medication adherence among patients with CVD and identify potential individual, behavioural and environmental factors predicting cardio-protective medication adherence. This study was the first to examine and compare medication adherence and predictive factors of adherence across different cultures and societies, in Australia and Iraq. The findings are valuable for shedding light on adherence attitudes and behaviours internationally and provide insights into medication adherence patterns of patients attending cardiac care services in tertiary hospitals in the different sociocultural and economic contexts of Middle Eastern and Western developed and developing countries. This study goes on to propose a pilot randomised controlled trial of a comprehensive multifaceted nurse-led medication adherence intervention for patients with cardiovascular disease, attending cardiac rehabilitation or out-patient cardiac clinics for secondary prevention services. The findings can be used as a source for future adherence studies in developed and developing countries, and across patient population with chronic conditions.

This study provides a systematic review of different evidence-based interventions to improve medication adherence among patients with cardiac disease, and suggests that nurse-led, multifaceted interventions have the best chance to optimise medication adherence. It adds to the body of existing research and provides a foundation for and refines adherence enhancing approaches. It generates new insights and offers and important basis for developing behaviour change interventions that effective in cardiac patients with poor medication adherence.

A strength of this study is also derived from the use of multi-centre comparison methods: using the same survey in two sites. Findings provide new knowledge of the problem of medication non-adherence among patients from different socio-eco-cultural contexts: Australia and Iraq. To our knowledge, this study is the first to use multiple medication adherence instruments on patients from tertiary hospitals in Australia and Iraq. However, these adherence measures did not distinguish between specific cardiac medication classes but rather medication adherence behaviour generally (Crowley et al. 2015). Future studies should consider the effects for individual classes of medication. There are limited validation and reliability data on the instruments used in the study, which may limit confidence in their ability to accurately indicate patients' adherence to their medications. Therefore, it would be worthwhile exploring alternative approaches to assess medication adherence, and potentially predictive factors. Further, qualitative approaches may provide greater details and understanding, since they can explore in greater depth the wide variety of factors that might be important than a structured survey cannot reveal.

A limitation of this study is that it was conducted in one single tertiary hospital in Australia and three hospitals in Iraq. Differences between site sample sizes may have limited the ability to determine significant inter-site differences. However, convenience sampling from multiple sites may also have allowed the sample to better represent these populations with regard to demographic characteristics. The results of the present study may have been more comprehensive if the study had recruited in other public hospitals in Australia, obtained a larger sample size and employed random sampling. The study recruited participants using a convenience sampling strategy and it is therefore unclear to what extent findings can be generalised. This study was conducted in busy clinical cardiac settings where the patients were asked to complete study questionnaires shortly after their cardiac rehabilitation session or cardiac clinics visits or (in the ward) when deemed clinically stable. This may have limited their responses. This study relied on findings using survey design. A cross-sectional study design prevents any claim of causality between adherence and its predictors (Polit & Beck 2008). Use of self-report questionnaires might have biased the study findings, with responses potentially influenced by social desirability, as is the case with many studies on medication adherence (Morisky & DiMatteo 2011).

Differences in sociodemographic characteristics and some health-related variables between Australian and Iraqi samples, while intrinsic to the study, may have limited the interpretation of comparative findings. For future study, it would be worthwhile to employ mixed-methodology to include a qualitative approach that could explore predictors thoroughly, as qualitative approaches are able to provide more in-depth understanding than structured surveys. For the future, applying the proposed pilot RCT of nurse-led, multifaceted intervention using a mixed method design will clarify facets of low adherence to cardiac medications. However, the use of a multi-faceted intervention, while recommended as likely to increase the success of intervention as a whole, challenges researchers to identify the contribution of the individual components. This study will attempt to address this by seeking participants' experiences of each separate component of the intervention. Overall, this study sets out the essential first steps for what may be an exciting new development in the contribution of nursing staff to delivering a substantial benefit to a sizeable patient group where there is clear potential for significant improvement in adherence.

6.7 Chapter Summary

This chapter discussed the findings of the study in relation to the levels of medication adherence and significant predictive factors affecting adherence among patients with cardiovascular disease in Australia and Iraq. This chapter also discussed a proposed multi-faceted medication adherence intervention comprising motivational interviews and text message reminders to improve adherence to cardiac medication regimes by targeting individual behaviour change. The results of the study were reviewed, analysed and compared using the lens of the Theory of Planned Behaviour (TPB) (Ajzen 1991).

The study demonstrated that adherence to cardiac medications in both Australian and Iraqi patients with CVD was suboptimal, with more Iraqi patients reporting lower levels of adherence than patients from Australia. The prevalence of non-adherence in both countries was linked to the factors predictive of medication adherence, which were, for both groups, the ability to self-administer and refill medication and beliefs about the necessity of cardiac medications. The study analysis revealed that patients' socio-eco-cultural characteristics may also have potential to affect medication adherence. Based on the survey results, this study proposes a fully developed protocol that is suitable for testing the effectiveness of evidence-based, nurse-led intervention to improve adherence to medications in patient with CVD at different stages of their disease. The next chapter examines the conclusion, implications and recommendations of this study.

CHAPTER 7 Conclusion of the Study

7.1 Introduction of the Chapter

This chapter provides the conclusion of the thesis and discusses the implications and recommendations of the study findings for nursing practice and policy, education and future research. It identifies the unique contribution of the work to the literature and to nursing science and indicates it's a contribution to future policies for Australia and Iraq and also for other major cardiac care settings in developed and in Middle Eastern nations with similar socio-eco-cultural contexts.

This thesis includes the first study to report and compare cardiac medication adherence behaviours from patients in both developed and developing countries: Australia and Iraq. The findings both the Australian and Iraqi cohorts demonstrated suboptimal medication adherence among patients admitted to cardiac wards and to those attending for out-patient cardiac services. Iraqi patients had significantly lower levels of medication adherence compared to patients from Australia. This study examined and compared socio-demographic, health-related, attitudinal and behavioural factors potentially predictive of medication adherence in these countries using the lens of the Theory of Planned Behaviour (TPB) (Ajzen 1991). Study findings demonstrated that ability to self-administer and refill medications, and positive beliefs about the necessity of medication were independently predictive of cardiac medication adherence in patients with CVD. Study findings highlight the need to enhance adherence to medication by utilising strategies that address patients' ability to refill medication and target their beliefs or misperceptions about cardiac medications.

The thesis also includes a systematic review of the effectiveness of interventions on medication adherence; findings indicate that interventions which comprise motivational interviewing counselling and text message reminders have significantly potential to improve medication adherence in patients with CVD. Survey findings can be employed to inform content of the motivational interviewing counselling, which should address the patients' ability to correctly self-administer and refill medications and should address their beliefs and any misperceptions about cardiac medications, taking into consideration their socioeconomic and cultural contexts. Finally, a test of a multifaceted intervention which can be delivered by nurses is proposed using a pilot RCT, as it is believed this approach can have a positive impact on medication adherence of patients with CVD.

7.2 Implications of the Study Findings

With the increasing prevalence of CVD and the associated disease burden in Australia and Iraq, it is crucial for healthcare providers including clinical nurses to enhance medication adherence among this population to promote secondary preventive approaches to improve health outcomes at all points in the journey of patients with CVD. Cardiac patients at different points of their disease journey, in both Australia and Iraq were showed to have unacceptable levels of medication adherence. Medication adherence was shown to be affected by individual, attitudinal and behavioural factors (the ability to self-administer and refill medications and beliefs about medications as well as organisational factors such as the location of CVD services (cardiac ward versus cardiac clinics, a proxy for differing time points in the cardiac patient journey). Despite the differences in socio-economic and cultural characteristics, the findings indicate similarities in non-adherence behaviours and predictive factors from patients in Australia and Iraq. Findings may also be relevant to patients of other similar countries: other Middle Eastern countries as well as developed countries with multicultural populations. The results of this study have implications for education and clinical practice, policy makers and managers, and future research.

7.2.1 Implications and Recommendations for Clinical Practice

Study findings indicate that the problem of medication non-adherence is evident at multiple time points in the patients' journey with CVD: prior to an acute event (and hence reported by hospital in-patients) and post hospital discharge (when attending cardiac rehabilitation and out-patient follow-up). Study findings demonstrate that the problem of medication non-adherence must be addressed at every therapeutic opportunity in the patient journey.

Study findings demonstrate for clinicians the importance of fulfilling their roles in assessment of their patients' medication adherence status (Joosten et al. 2008). Healthcare providers, including clinical nurses, need to understand that failure to achieve optimal control of cardiac disease may be linked to inadequate medication self-management. Study findings indicate that clinicians should be encouraged to address patients' self-management needs and any concerns related to aspects of their medication regimes. Some patients may be harbouring concerns about their medications yet hesitate to raise these concerns. Survey findings identified factors that predicted medication adherence in patients with CVD in Australia and Iraq. In both countries, no previous studies had evaluated factors predicted of medication adherence for these patient groups. This study has therefore, provided clinicians with information to guide clinical practice which was not available before.

Study findings also provide evidence that adherence to cardiac medication regimes are likely not due to a single underlying factor, whether that be demographic, medical, psychological, or beliefs about medication. Rather, based on the current study findings, medication non-adherence may be the result of multiple factors, intentional and non-intentional, including the inability to self-administer and refill medication, inability to plan their medication refilling, and medications costs. Further, adherence to medications may be influenced by beliefs regarding perceived medications harm or perceived medications overuse or over prescription. Also, findings suggest there may be differences in medication adherence attitudes and behaviours at different points in the cardiac journey (represented by recruitment from cardiac wards versus cardiac out-patient clinics).

Systematic review findings demonstrated that nurse-led interventions that can improve medication adherence among patients with CVD are limited, yet potentially valuable. Review findings also supported the potential effectiveness of multi-faceted strategies to improve medication adherence focused on patient medication adherence self-management led by nurses. This research offers useful information to help clinicians in delivering effective interventions to improve medication adherence among patients with CVD. In both Australia and Iraq, nurses need to be prepared during their training and practice to carry out this role in order to support medication adherence. The role of nurses to improve medication adherence and the emphasis upon this during nurse training and clinical practice should be oversighted by hospitals to determine whether and how these nursing roles can be implemented. Clinical nurses need to build trust with their cardiac patients in order to be able to proactively address any belief-related adherence barriers arising as a result of miscommunication. An effective care provider-patient relationship may be an important component to build an encouraging environment to achieve treatment plan goals (Brown & Bussell 2011). Cultural differences in health beliefs and practice, in particular in relation to taking medications, may have important implications for discussions about medications between patients and healthcare professionals, and in reaching shared decisions about medication adherence.

Recommendations for Clinical Practice

It is therefore, recommended that:

- Timely recognition of medication adherence issues and using appropriate interventions targeting predictive factors of non-adherence are likely to increase medication adherence leading to improve patients' health outcomes, quality of life and unnecessary hospital admission.
- Nurses need to understand the impact of cultural background on patients' perceptions and beliefs about medication and include medication-related consultation in their patient education.
- Reminders interventions using text messages or phone calls using smartphone or tablet devices, all deliverable by nurses, have been found useful in improving adherence to medication in patients with CVD.

Nurse-led motivational interviewing counselling and text message reminders may be recommended to the clinical setting as effective medication adherence strategies in the cardiac rehabilitation and out-patient settings.

7.2.2 Implications and Recommendations for Education

This research offers useful information to support education of healthcare staff such as nurses in delivering effective interventions to improve medication adherence among patients with CVD. Professional continuing education and in-service training on the significance of secondary prevention of cardiac disease should be provided to nurses so that they are equipped with the necessary knowledge, attitudes and skills for assuming this within clinical nursing roles. Patients should receive medication education sessions, and face to face counselling integrated into their care plans to enhance their ability to refill medications and to strengthen their beliefs about cardiac medications. Medication education and counselling may provide patients with useful knowledge and strategies to manage their medication adherence behaviours, hence promoting the effectiveness of cardiac medications and patients' health. The reinforcement of medication importance during acute admissions, during cardiac rehabilitation and in routine follow up visits may improve medication refill compliance and resolve misperceptions about cardiac medications. Establishing medication adherence intervention plans for patients in cardiac care settings will help nurses determine the degree of probability of non-adherence to medications. Based on this study findings, multifaceted interventions can be delivered in the form of individualised interventions to enhance patients' medication adherence.

When deciding what combination strategy to use in an intervention, the appropriateness of interventions needs to be assessed and suitable choices made bearing in mind individual patient needs, the context and culture, and local resources available. If clinical nurses are to include in their roles counselling patients on how to improve adherence to treatment, their training needs to include training on motivational interviewing techniques. As nurses have a vital role in patient education, promotion of medication adherence can make a valuable contribution through provision of necessary information to support patients' adherence. In addition, nurses' role in promoting adherence can involve sending text message reminders and establishment of a routine to facilitate medication adherence, and training as well as resourcing will be required to enable this. Nurses will also require medication education targeting practical medication management skills, including the ability to self-administer and setting plans to refill medications before runout (Rueda et al. 2006). More attention on the role of cardiac nurses in assessing patients' cardiac medication self-management could enhance the nurses' role in cardiac rehabilitation.

Recommendations for Education

It is therefore recommended that:

- Medication education can be promoted at undergraduate (pre-registration) and post-qualification levels to support development of specialist skills and knowledge.
- Inter-professional medication education should provide opportunities for clinical nurses, pharmacists, and physicians to learn with, from and about each other and to develop the knowledge, skills and attitude required to support medication adherence amongst patients with CVD.
- Comprehensive medication education must be delivered, and medications dispended with detailed and explicit instructions on administration, on the

bottle/package where possible, to help patients remember and follow the recommendations correctly, with written instructions to refer to when needed.

- Individualised and group education sessions should be provided for cardiac patients by clinical nurses, including reviewing their medication adherence, and supplying written summaries of the sessions.
- Intervention of medication adherence interventions such as motivational interviewing and text message reminders will require that nurses are educationally prepared and enabled to operate within an appropriate professional framework (including, for example, supervisory support) for effective delivery of appropriately targeted individual plans of care for patients with CVD.

7.2.3 Implications and Recommendations for Managers and Policy Makers

This study revealed poor medication adherence and relationships between the level of cardiac medication adherence, the ability to self-administer and refill medication and beliefs about medication. Medication adherence should be recognised as an essential focus throughout the cardiac patient journey, and policy makers should establish measures to support this as a priority. In Iraq, no existing policies have been developed by professional nursing organisations and it is not clear how effective are the Australian cardiac rehabilitation guidelines and associated policies for the role of clinical nurses in patient medication education. Lack of relevant out-patient or cardiac rehabilitation policies or position statements from professional nursing organisations has significantly contributed to the lack of understanding of the nurses' role of medication education in cardiac rehabilitation, in Australia and particularly in Iraq. Therefore, there is urgent need to develop policies and position guidelines for out-patient cardiac care and secondary prevention for healthcare providers, including nurses. Clinical nurses should actively take part in this policy-making process and play an integral role in advisory committees.

Policies or guidelines regarding medication adherence assessment and interventions should also be established in hospitals to guide healthcare providers in promotion of adherence in out-patient cardiac clinics as well as in-patient cardiac wards. Further, an international cardiac rehabilitation and secondary prevention network should be established for nurses to promote communication among nurses in the area of medication adherence interventions. When considering components to include in behaviour change strategies, policymakers need to combine evidence from the full range of methods available. There is a great need for nurses and nurse leaders in Australia and Iraq to inform government and policy makers of the importance of the development of medication adherence case management system as well as the provision of opportunities for nurses to take on expanded or extended roles in improving adherence to provide more cost-effective care for patients.

Recommendations for Policy Makers:

It is therefore recommended that:

- Given the various predictive factors that contribute to non-adherence, achieving meaningful gains will undoubtedly require policymakers to develop, rigorously evaluate, and systematically deploy strategies that address key patient, clinician, and health system factors such as patients' ability to self-administer and refill medication and their beliefs about medications, patient-provider miscommunications, and patients' ability to access cardiac care settings.

- Policies should be developed in collaboration between nurses, physicians, cardiologists and pharmacists to keep medications at minimum dosage, negotiating priorities with patients, providing education, monitoring adherence to medication at appointments and reinforcing the patients' efforts to adhere at each visit, including providing practical assistance where required (Lerman 2005).
- Policies should enable and support patients with the ability to self-administer and refill medications to be adequately prepared to do so, with meticulous monitoring of their medication adherence.
- Policies should support models of care that place emphasis on individual patient care and consumer participation, facilitating patient involvement in decision making about their medications, reinforcing patients' ability to self-administer and refill their medication, addressing patient beliefs and perceptions about prescribed medications.
- Policies should mandate simplification of prescribed regimes to minimum dosing.

7.2.4 Implications and Recommendations for Future Research

This study addressed the levels of medication adherence of patients with CVD in tertiary hospitals in Australia and Iraq, examining relationships with predictive factors of medication adherence. Findings from this study informed the development of a nurse-led medication adherence intervention proposal, which uses a multifaceted approach, employing motivational interviewing counselling and text message reminders. Future research is suggested to test the feasibility, acceptability to staff as well as patients, effectiveness and cost-effectiveness of the proposed intervention. This study confirms that future research is needed to create and use different strategies of medication adherence counselling and education for patients with CVD who are assessed to be non-adherent to medication regimes. The study suggests that research is urgently needed to develop formal methods for combining evidence from different types of evaluation to arrive at judgments concerning the likely effective combinations tailored to target attitudes and behaviour, tailored to individual need and context.

Further study is required to add detail to the patterns of non-adherence by specifying the effects for individual classes of cardio-protective medications, and to study longer term effects of medication adherence interventions on morbidity and mortality rates. Qualitative investigation is suggested for detailed exploration of the phenomenon of adherence, to achieve in-depth understanding of predictive factors beyond non-adherence behaviours. Further studies could be designed, focusing on larger sample size, investigating more individual, socioeconomic, and cultural factors affecting long-term medication adherence, and the development of more effective intervention strategies in the area. Investigations should target medication adherence of patients with CVD at different points in the cardiac trajectory, including early and late stages patients care. Further, work should explore the influence of culture and ethnicity in relation to medication adherence, and how this relates to development of counselling and education.

The generalisability of findings could be enhanced by researchers working with more diverse populations and by expanding the sampling to include patients in other cardiac programs at a wider variety of hospitals, including large urban, suburban, or rural hospitals. Future research in Australia and Iraq should exploring the cost-effectiveness of different models of counselling and education delivery, including integrating primary and secondary preventive care to provide seamless service and maximise efficient use of resources. Future research needs to further explore culture-related issues of medication adherence, including the ability to self-administer and refill medications and beliefs about medication. Further research is needed to improve the understanding of the impact of cultural background on patients' attitudes in taking medication and this knowledge might be used to improve the delivery of cardiac care by clinical nurses.

Recommendations for Future Research

- Nurse-led and nurse-collaborative interventions have the capacity to improve medication adherence among patients in the community, this should be tested by well-designed studies using highly reliable tools for measuring medication adherence.
- Nurse-led interventions to improve adherence to cardiovascular medications, multifaceted interventions appear to offer the best opportunities to optimise medication adherence, with component behavioural interventions in the form of motivational interviewing, educational content, text and/or phone messaging showing the greatest success.
- The proposed pilot RCT in this study was designed to employ valid and reliable instruments with Arabic translation that will be useful for future research in Arabic speaking populations in order to assess the levels of cardiac medications adherence and factors predictive of adherence.
- Combine instruments used in the study with other methods of assessing cardiac medications adherence and related behaviours to strengthen study rigor.
- Explore the issues surrounding culture and perceptions of treatment, such as the possible role of cultural background on beliefs about adherence to medications.

- Exploring possible solutions for improving the ability to self-administer and refill medication and address patient beliefs about the necessity of taking cardiac medication in multi-cultural contexts.
- Use qualitative methodologies for detailed and in-depth exploration of patients' ability to self-administer and refill medication, their beliefs about their cardiac medications and any other factors related to their medication adherence.
- Continue to identify groups of patients with CVD who are at greater risk of poor adherence to their secondary prevention medications and are therefore most likely to benefit from more intensive educational or counselling intervention.
- Further explore the impact of the healthcare provider–patient relationship on medication adherence, exploring this issue from these two different perspectives.

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Appendix A Characteristics of Included Studies Table

Supplemental File 1

Table S1: Characteristics of included studies based on the Cochrane Collaboration's tool for assessing the risk of bias

Beune et al. (2014)		
Methods	**Study design**: Cluster Randomised Trial **Country**: Netherlands **Dates patients recruited**: No record **Maximum follow-up**: 6 months	
Participants	**Inclusion criteria**: aged 20 years or older, diagnosis of Hypertension (HTN) and having SBP ≥140 mmHg at the last office visit. **Exclusion criteria**: Patients with type 1 or type 2 diabetes, patients whom they judged unfit to participate in the study. **N randomised**: total: 146; intervention: 75; control: 71 **Diagnosis of Patients (% of pts):** HTN: 100%	
Interventions	**Intervention**: Nurse-led Culturally Adapted Hypertension Education (**CAHE**): three structured 30 minutes culturally appropriate counselling sessions at 2 weeks, 8 weeks & at 20 weeks, and then written educational materials. **Components**: Educational & behavioural counselling **Setting**: Primary care centres **Total duration**: 6 months **Control Group**: usual hypertension care	
Outcomes	Medication adherence Outcomes Measured at 6 months, post intervention	
Source of Funding	ZonMw, the Netherlands organisation for health research and development	
Conflict of interest	None declared.	
Notes	No significant difference between groups for self-reported medication adherence	
Risk of Bias		
Bias	**Authors' Judgment**	**Support for judgment**
Random Sequence Generation (Selection Bias)	Low risk	Patients were enrolled and assigned to either the intervention or the control group using a computer-generated randomisation list.
Allocation concealment (Selection Bias)	Low risk	It was possible to conceal the allocation of the intervention from the health centres and care providers due to the nature of practice-based intervention.

Blinding of participants and personal (performance bias)	High risk	Patients and nurses are not blinded due to the behavioural nature of intervention.
Blinding of outcome assessment (detection bias)	Low risk	The trained research assistants who performed the baseline and follow-up assessments were blinded. Also, the statistician who analysed the data was blinded to the intervention assignments
Incomplete outcome data (Attrition bias)	Low risk	Dropouts were equal across groups. Reasons supplied for the patients who did not complete the intervention. 95% of patients followed up at 6 months.
Selective reporting (reporting bias)	Low risk	All pre-specified (primary and secondary) outcomes have been reported in previous study protocol.
Group balance at baseline	Low risk	The baseline characteristics for both groups were similar except for medication prescription and insurance status.
Intention to treat analysis conducted	Low risk	All data were analysed in terms of intention to treat.
Groups receive same treatment (apart from the intervention)	Low risk	Both groups treated equally except for the intervention.

Guirado et al. (2011)	
Methods	**Study design**: multi-centre, cluster-randomised trial **Country**: Spain **Dates patients recruited**: no records **Maximum follow-up**: 12 months follow-up
Participants	**Inclusion criteria**: 1) Patients with hypertension 2) aged 18–80 years 3) visiting the clinic for long-term follow-up and control of hypertension using anti-hypertensive drug therapy and, 4) had attended the clinic for a minimum period of 6 months. **Exclusion criteria**: Individuals who had serious psychiatric, physical, or sensory alterations. **N randomised**: total: 996; intervention group = 515; control group = 481. **Diagnosis of Patients (% of pts):** Hypertension: 100%
Interventions	**Intervention**: Personalised information by a trained nurse and written leaflets: **Intervention group** received education using the standardised guidelines developed for the intervention. Each visit lasted for an average of 15 minutes. The information provided to the patient was personalised according to the needs of the patient. A schedule sheets with the treatment plan were provided, which contained information on the drugs prescribed, the dosage and schedule, and basic advice on how to maximise the treatment schedules. The purpose of these sheets was to reinforce the nurse's verbal instructions and advice to the patient. **Components**: Educational counselling. **Setting**: primary healthcare centre.

	Total duration: 12 months. **Control Group**: Received usual clinical care.	
Outcomes	Self-reported adherence to the medication measured by the Haynes-Sackett and Morisky-Green tests. Outcomes Measured at 12 months.	
Source of Funding	The Fundación Jordi Gol i Gurina. The present study was funded by a grant from the Agency for the Evaluation of Medical Technology and Research. Also, support from the Instituto de Salud Carlos III is acknowledged.	
Conflict of interest	None declared.	
Notes	The educational intervention had no significant impact on patients' adherence to the medication.	
Risk of Bias		
Bias	**Authors' Judgment**	**Support for judgment**
Random Sequence Generation (Selection Bias)	High risk	Randomisation was by primary care centre.
Allocation concealment (Selection Bias)	Unclear risk	The allocation concealment was not described.
Blinding of participants and personal (performance bias)	High risk	The blinding process was not described.
Blinding of outcome assessment (detection bias)	High risk	Blinding for medication adherence assessment was not described.
Incomplete outcome data (Attrition bias)	Low risk	Dropouts across groups was described 79 patients in the intervention group and 49 patients in the control group (Figure 1).
Selective reporting (reporting bias)	Unclear risk	No protocol available; it is difficult to determine this without a protocol.
Group balance at baseline	Low risk	No significant differences were observed among groups (Table 1).
Intention to treat analysis conducted	Low risk	Yes.
Groups receive same treatment (apart from the intervention)	Low risk	Each treated equally except for the intervention.

Hacihasanoğlu & Goözuöm (2011)		
Methods	**Study design**: Randomised Controlled Trial **Country**: Turkey **Dates patients recruited**: February–November 2006 **Maximum follow-up**: 9 months	
Participants	**Inclusion criteria**: aged 35 years or older, diagnosis of Hypertension (HTN) one year prior to study entry, prescribed antihypertensive medication, literate, able to communicate easily and cooperate with researchers **Exclusion criteria**: Patients who have any disease or condition (e.g. diabetes mellitus, heart failure, renal impairment). **N randomised**: total: 120; intervention A: 40; intervention B: 40; control: 40 **Diagnosis of Patients (% of pts):** HTN: 100%	
Interventions	**Intervention**: Nurse-based educational intervention & in-home monitoring for medication adherence: three groups A, B, & control group. Groups A & B received a total of six-monthly education sessions about medication adherence. Group B also received individual & structured educational phone call about healthy lifestyle behaviours. **Components**: Educational & behavioural counselling. **Setting**: Public primary health care facilities. **Total duration**: 9 months **Control Group**: Usual hypertension care.	
Outcomes	Medication adherence and lifestyle behaviours Outcomes Measured at monthly based for 9 months.	
Source of Funding	No record	
Conflict of interest	None declared.	
Notes	Intervention groups had average scores of medication adherence & were significantly higher than control group.	
Risk of Bias		
Bias	**Authors' Judgment**	**Support for judgment**
Random Sequence Generation (Selection Bias)	High risk	Randomisation was provided by enrolling the patients into Group A on Monday, into Group B on Tuesday and into Control group on Wednesday and so on. To prevent bias, following week days were changed.
Allocation concealment (Selection Bias)	High risk	In adequate concealment of allocation prior to assignment.
Blinding of participants and personal (performance bias)	High risk	Allocation and outcomes data were not blind.
Blinding of outcome assessment (detection bias)	Low risk	The authors stated that Statistician was blinded.

Incomplete outcome data (Attrition bias)	Low risk	Dropouts were equal across groups and the description of withdrawals from the study were given. No losses to follow up.
Selective reporting (reporting bias)	Low risk	All outcomes were reported at all time points.
Group balance at baseline	Low risk	At baseline the two groups were well balanced in terms of demographic and clinical characteristics and prescribed antihypertensive medication.
Intention to treat analysis conducted	High risk	No.
Groups receive same treatment (part from the intervention)	Low risk	Patients in the 3 groups were monthly followed-up by phone call. The researcher telephoned contact groups A and B to give them general information about hypertension and to remind them about visit dates. Monthly visit was also conducted with the control group for the recording of blood pressures and weight. Control group was routinely monitored in health care facilities with the control group, giving general advice on any problems encountered and encouraging and supporting appropriate actions.

Ho et al. (2014)	
Methods	**Study design**: Randomised Clinical Trial **Country**: United States **Dates patients recruited**: 2 sites: July, September (2010); 1 site: July (2011) **Maximum follow-up**: 1 year
Participants	**Inclusion criteria**: patients' diagnosis of Acute Coronary Syndrome (ACS). **Exclusion criteria**: (1) patients admitted for primary non-cardiac diagnosis who developed ACS as a secondary condition (e.g. perioperative MI); (2) planned discharge to nursing home or skilled nursing facility; (3) irreversible, non-cardiac medical condition (e.g. metastatic cancer)likely to affect 6-month survival or inability to execute study protocol; (4) lack of telephone or cell phone; (5) VA not a primary source of care in the future; (6) fill medications at non-VA pharmacy; and (7) pregnancy. **N randomised**: total: 241; intervention: 122; control: 119 **Diagnosis of Patients (% of pts):** ACS: 100%
Interventions	**Intervention**: Simple direct-to patient intervention: two mailed communications: identical information about the importance of lifetime use of β-blockers following MI & that adverse effects can be managed & the importance of remembering to refill medication. **Components**: Educational & behavioural counselling **Setting**: Department of Veterans Affairs medical centres **Total duration**: 1 year

	Control Group: usual care	
Outcomes	Medication adherence for 4 cardio-protective medications. Outcomes Measured during the 365-days follow-up.	
Source of Funding	Funded by a Veterans Health Administration Health Service Research & Development (HSR&D) Investigator Initiated Award	
Conflict of interest	None declared.	
Notes	Intervention group had greater proportion of adherent compared with control group.	
Risk of Bias		
Bias	**Authors' Judgment**	**Support for judgment**
Random Sequence Generation (Selection Bias)	Low risk	Eligible patients randomised using blocked randomisation stratified by study site in a 1:1 ratio to intervention or control group.
Allocation concealment (Selection Bias)	Low risk	The allocation sequence was concealed until a patient consented to participate and was generated centrally using the graphical user interface implemented for the study.
Blinding of participants and personal (performance bias)	Unclear risk	Blinding processes was not described. No description of who was or was not blinded.
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessment was performed by someone blinded to study group assignment.
Incomplete outcome data (Attrition bias)	Low risk	Dropouts were equal across groups (patient flowchart) and the description of drop-out from the study were given. No description for the percentages of the lost to follow up at the end of the study.
Selective reporting (reporting bias)	Low risk	All medication adherence and clinical endpoints were reported during the 365-days follow-ups.
Group balance at baseline	Low risk	Baseline characteristics of the patients were comparable (Table 1).
Intention to treat analysis conducted	Low risk	Intention to treat analysis was used for all analyses.
Groups receive same treatment (apart from the intervention)	Low risk	Consistent with usual practices at each site, patients in both groups received standard ACS hospital discharge instructions. After randomisation, both intervention and usual care patients were scheduled for a 12-month clinic visit.

Jiang et al. (2007)		
Methods	**Study design**: Randomised Controlled Trial **Country**: China **Dates patients recruited**: September 2002 to December 2003 **Maximum follow-up**: 6 months	
Participants	**Inclusion criteria**: (1) first hospitalization with either angina pectoris or myocardial infarction; (2) willing to participate in this study; (3) able to speak, read and write Chinese; (4) living at home with family after hospital discharge; and (5) available for telephone follow-up. **Exclusion criteria**: (1) planning for surgical treatment; (2) with pre-existing mobility problems; (3) with hypothyroidism or nephrotic syndrome; (4) with diagnosed psychosis or currently undergoing antipsychosis treatment; and (5) with terminal illness. **N randomised**: total: 167; intervention: 83; control: 84 **Diagnosis of Patients (% of pts):** Coronary heart disease	
Interventions	**Intervention**: Nurse-led cardiac rehabilitation program: a 12-week hospital-initiated home-based multifaceted cardiac rehabilitation intervention consist of 2 phases (1): Hospital-based patient/family education & (2): Home-based rehabilitative care. **Components**: Educational & behavioural counselling **Setting**: 2 tertiary medical centres. **Total duration**: 6 months. **Control Group**: the routine care	
Outcomes	Medication adherence. Outcomes Measured at 3 & 6 months follow-up.	
Source of Funding	The Hong Kong Polytechnic University, Hong Kong, China.	
Conflict of interest	None declared.	
Notes	Intervention group had a better medication adherence from baseline to 6 months compared with control group.	
Risk of Bias		
Bias	**Authors' Judgment**	**Support for judgment**
Random Sequence Generation (Selection Bias)	Low risk	Patients were randomly allocated using computer-generalized random table.
Allocation concealment (Selection Bias)	Unclear risk	Allocation concealment was not described.
Blinding of participants and personal (performance bias)	Low risk	Two research assistants were blinded to patient group assignment however, the authors did not described blinding for patients.

Blinding of outcome assessment (detection bias)	Low risk	One research assistants was blinded for conducting the outcomes assessment.
Incomplete outcome data (Attrition bias)	Low risk	Reasons for the patients who did not complete the intervention are given. A total of 151 and 141 patients completed the study respectively, followed up at 3 and 6 months.
Selective reporting (reporting bias)	Unclear risk	All outcomes were reported at all time points. However, medication adherence was assessed as a whole in this study, which makes it difficult to explain the change of physiological risk parameters such as BP at six months.
Group balance at baseline	Low risk	No significant difference was found between the intervention and control group. The demographic and clinical characteristics of the patients were comparted at baseline (Tables 1 and 2).
Intention to treat analysis conducted	Low risk	The examination of the intervention effect was conducted on an intention-to-treat basis.
Groups receive same treatment (apart from the intervention)	Low risk	Groups were treated equally except for the intervention.

Kripalani et al. (2012)	
Methods	**Study design**: Randomised Controlled Trial **Country**: United States **Dates patients recruited**: between March 2004 and March 2005 **Maximum follow-up**: 12 months
Participants	**Inclusion criteria**: Patients with established CHD, ≥ 18 years of age, regularly filled their prescriptions in the health system pharmacy, African-American, female, and of low socio-economic status. **Exclusion criteria**: Patients routinely receiving caregiver assistance with medication management, already using a medication chart similar to the intervention, corrected visual acuity worse than 20/60, inability to communicate in English, no telephone, no mailing address, police custody, lack of cooperation, psychiatric illness, delirium or severe dementia, being too ill to participate, or previous enrolment in the study. **N randomised**: total: 440; intervention: refill reminder postcard: 103, illustrated medication schedules: 124, both refill reminder postcard & illustrated medication schedules: 117; control: 96. **Diagnosis of Patients (% of pts):** CHD: (100%).

Interventions	**Intervention**: Graphically Enhanced Interventions: 4 groups: 1) patients received usual care, 2) refill reminder postcards, 3) illustrated daily medication schedules, or 4) both interventions for one year after completed a 30–45 minute interviewer assisted questionnaire. **Components**: education & Behavioural intervention. **Setting**: primary care clinics. **Total duration**: 12 months. **Control Group**: NR.	
Outcomes	Cardiovascular medication refill adherence. Outcomes Measured at 12 months follow-up.	
Source of Funding	No record	
Conflict of interest	None declared.	
Notes	The interventions did not improve adherence overall. Adherence did not differ significantly across treatments.	
Risk of Bias		
Bias	**Authors' Judgment**	**Support for judgment**
Random Sequence Generation (Selection Bias)	Low risk	Patients were randomised using a computerised random number generator.
Allocation concealment (Selection Bias)	Low risk	Each treatment assignment was sealed in an opaque envelope for concealment of treatment allocation.
Blinding of participants and personal (performance bias)	High risk	Patients and treating physicians were not blinded.
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded.
Incomplete outcome data (Attrition bias)	High risk	12 months: 5/344 missing from intervention groups (withdrawal from the study) and 12/344 missing (insufficient refill data), and 3/96 missing from control group (due to insufficient refill data).
Selective reporting (reporting bias)	Unclear risk	No protocol available, although it appears that all outcomes are reported it is difficult to determine this without a protocol.
Group balance at baseline	Low risk	No significant differences in baseline characteristics were present across treatment groups (Table 1).
Intention to treat analysis conducted	Low risk	Yes.
Groups receive same treatment (a part from the intervention)	Low risk	The 3 intervention groups received different interventions: 1) patients received usual care, 2) refill reminder postcards, 3) illustrated daily medication schedules, or 4) both interventions

Leiva et al. (2014)		
Methods	**Study design**: Multicentre parallel Randomised Controlled Trial **Country**: Spain **Dates patients recruited**: between February 2011 & September 2013 **Maximum follow-up**: 12 months	
Participants	**Inclusion criteria**: Patients aged 18–80 years with uncontrolled essential hypertension. **Exclusion criteria**: Patients with non-essential hypertension; those undergoing hemodialysis; institutionalized or terminally ill patients; and those unwilling to provide informed consent. **N randomised**: total: 223; intervention: 114; control: 109 **Diagnosis of Patients (% of pts):** uncontrolled essential hypertension: (100%)	
Interventions	**Intervention**: Brief Multifactorial adherence based intervention: motivational interviewing, pillbox reminders, family support, BP measurements & antihypertensive reminder forms, & simplification of dosing regime. **Components**: Behavioural counselling **Setting**: 2 primary care centres. **Total duration**: 12 months. **Control Group**: did not receive any change in their care. However, they were contacted at baseline and at 12 months and asked to complete the same measurements and interviews as the intervention group.	
Outcomes	Systolic & diastolic BP Medication adherence. Outcomes Measured at 1, 3 & 9 monthly follow-up.	
Source of Funding	The Carlos III Health Institute of the Ministry of Economy and Competitiveness of Spain.	
Conflict of interest	None declared.	
Notes	No significant difference of adherence to anti-hypertensive medication observed at 12 months between groups.	
Risk of Bias		
Bias	**Authors' Judgment**	**Support for judgment**
Random Sequence Generation (Selection Bias)	Low risk	The patients were allocated using a computer-generated allocation sequence with a block size of eight.
Allocation concealment (Selection Bias)	Low risk	Allocation concealment was centralised at a single coordinating centre.
Blinding of participants and personal (performance bias)	Low risk	Patients and nurses could not be blinded to the patient allocation due to study procedures.

Blinding of outcome assessment (detection bias)	Low risk	The statistician and the physicians were blinded to patient allocation, and the main outcome was assessed by an external nurse blinded to patient allocation.
Incomplete outcome data (Attrition bias)	Low risk	Fairly equal dropouts across groups; reasons for dropouts Provided. At 12 months, 212 (89%) participants completed the study.
Selective reporting (reporting bias)	Unclear risk	All outcomes were reported at all time points. However, results show that differences in the application of the intervention and overestimation of its effects may have resulted in the absence of statistically significant differences between intervention and control groups
Group balance at baseline	Low risk	Patient characteristics at baseline were similar in the two groups (Table 1).
Intention to treat analysis conducted	Low risk	Yes.
Groups receive same treatment (apart from the intervention)	Low risk	Patients in both groups had two baseline visits 1 week apart and before study initiation to ensure that they met study criteria. Data were obtained at the second baseline visit and at 12-month follow-up. However, the level of care in the control group was positively influenced by participation in the trial.

Ma et al. (2014)	
Methods	**Study design**: Randomised Controlled Trial **Country**: China **Dates patients recruited**: between November 2011 & October 2012 **Maximum follow-up**: 6 months
Participants	**Inclusion criteria**: (1) patients older than 18 years who agreed to take part in the study; (2) patients diagnosed with essential hypertension by a cardiovascular physician; and (3) patients who took at least one antihypertensive medication. **Exclusion criteria**: (1) secondary hypertensive patients or (2) pregnant women. **N randomised**: total: 120; intervention: 60; control: 60 **Diagnosis of Patients (% of pts):** essential hypertension: (100%)
Interventions	**Intervention**: Motivational interview Counselling based on Social Cognitive Theory (SCT): (1) build rapport with the patients; (2) evaluate the patients' confidence and motivation for behaviour changes and their self-efficiency; (3) help the patients become aware of and address the ambivalence blocking their behaviour to change; (4) help the patients find the discrepancies between their values and their current behaviours; (5) provide strategies of adherence to behaviour changes; (6) summarise the pros and cons of the proposed behaviour changes; (7) set realistic and specific goals for behaviour modification; (8) prompt the

	patients to follow the plan for behaviour change; and (9) provide an overall summary of the MI session and the patients' performances. **Components**: Behavioural counselling **Setting**: 2 community health centres (1 hospital-based practice; 1 community-based practice). **Total duration**: 6 months. **Control Group**: hypertension information and recommendations to improve treatment adherence and change unhealthy lifestyles. The cardiologists or specialist nurses delivered a lecture on hypertension prevention for these patients every 6 weeks. The leaflets concerning hypertension information were freely delivered to the patients.	
Outcomes	Medication adherence. Outcomes Measured at baseline & 6 months follow-up.	
Source of Funding	No Records.	
Conflict of interest	None declared.	
Notes	The total scores and the mean scores of medication treatment & self-efficiency in the intervention group were higher than the scores of the control group over six months counselling.	
Risk of Bias		
Bias	**Authors' Judgment**	**Support for judgment**
Random Sequence Generation (Selection Bias)	Low risk	Patients were randomly allocated. Randomisation was performed by shuffling envelopes.
Allocation concealment (Selection Bias)	High risk	Participants were masked to the group assignment; however, the participating nurses were not blinded to the assignment.
Blinding of participants and personal (performance bias)	High risk	The nurse who delivered the MI counselling and usual care were not blinded to the sample allocation and these nurses are acquainted with one another.
Blinding of outcome assessment (detection bias)	High risk	The absence of a blinded condition may threaten its internal validity. In addition, the principal researcher played the role of both intervener and outcome assessor, which may have influenced participants to provide desired answers. The nurses who conducted the intervention and the usual care performed the outcome assessment.
Incomplete outcome data (Attrition bias)	Low risk	There was a small number of dropouts, evenly spread across the groups and reasons for dropouts Provided.
Selective reporting (reporting bias)	Low risk	The intervention protocol was established and all outcomes were reported at all time points.
Group balance at baseline	Low risk	There were no statistically significant differences in the demographic and clinical characteristics between the two groups (Table 1).
Intention to treat analysis conducted	High risk	No.

Groups receive same treatment (a part from the intervention)	Low risk	The patients of the two groups completed identical questionnaires in two phases. The follow up period was 24 weeks and completed. The second evaluation was conducted at week 24 (at the end of the intervention).

Nieuwkerk et al. (2012)		
Methods	**Study design**: Randomised Controlled Trial **Country**: Netherlands **Dates patients recruited**: from May 2002 to May 2004. **Maximum follow-up**: 18 months	
Participants	**Inclusion criteria**: Patients (aged ≥ 18 years) with indications for statin use (primary or secondary prevention of cardiovascular events). **Exclusion criteria**: Patients with severe fasting dyslipidemia (total cholesterol › 9.0 mmol/L or triglycerides › 4.0 mmol/L), fasting glucose › 7.0 mmol/L., patients who had used statins for › 3 months before inclusion, who had histories of drug and/or alcohol abuse, who were pregnant or breast-feeding, or who had life expectancies ‹ 2 years were excluded. **N randomised**: total: 201; intervention: 101; control: 100 **Diagnosis of Patients (% of pts):** coronary heart disease: (100%).	
Interventions	**Intervention**: Nurse-led multifactorial cardio-vascular risk-factor counselling: focused on changing modifiable risk factors such as increasing medication adherence. **Components**: Behavioural counselling **Setting**: 2 outpatient clinics. **Total duration**: 24 months. **Control Group**: multifactorial risk-factor counselling, during which the nurse practitioner explained the presence of unmodifiable risk factors, such as age, gender, and family history, and modifiable risk factors, such as lipid levels, diabetes mellitus, blood pressure, overweight, smoking habits, and physical activity.	
Outcomes	Medication adherence. Outcomes Measured at baseline & 3, 9, 18 months follow-up.	
Source of Funding	No records.	
Conflict of interest	None declared.	
Notes	Intervention group reported significantly higher levels of adherence to lipid lowering medication than patients in the control group.	
Risk of Bias		
Bias	**Authors' Judgment**	**Support for judgment**

Random Sequence Generation (Selection Bias)	Low risk	Patients were randomly assigned to intervention and control groups using a randomisation computer program
Allocation concealment (Selection Bias)	Unclear risk	Allocation concealment was not described.
Blinding of participants and personal (performance bias)	High risk	The study nurse was not blinded to the study groups and was responsible for the intervention for both groups.
Blinding of outcome assessment (detection bias)	Unclear risk	Insufficient information.
Incomplete outcome data (Attrition bias)	Unclear risk	Fairly equal dropouts across groups however, there was no description for patient who were lost to follow up.
Selective reporting (reporting bias)	Low risk	The study protocol was established. The medication adherence measure was described and the primary and secondary outcomes were listed in study methods in a pre-specified way. All primary and secondary outcomes were reported.
Group balance at baseline	Low risk	There were no significant differences in baseline characteristics between patients in the 2 study arms.
Intention to treat analysis conducted	Low risk	Yes.
Groups receive same treatment (apart from the intervention)	Low risk	At baseline, all patients completed a self-report related questionnaire. Patients completed the same questionnaire, which then also included questions about adherence to lipid-lowering medication and beliefs about medication.

Ogedegbe et al. (2008)	
Methods	**Study design**: Randomised Controlled Trial **Country**: United States **Dates patients recruited**: NR. **Maximum follow-up**: 12 months
Participants	**Inclusion criteria**: African American or black; age ≥ 18 years; diagnosis of hypertension; taking at least one antihypertensive medication; uncontrolled BP on two successive office visits before screening (BP ≥140/90 mm Hg or ≥130/80 mm Hg for those with kidney disease or diabetes); and fluency in English. **Exclusion criteria**: NR **N randomised**: total: 190; intervention: 95; control: 95. **Diagnosis of Patients (% of pts):** hypertension: (100%).

Interventions	**Intervention**: Motivational interviewing (MINT) for improving medication adherence: MINT group received behavioural counselling about medication adherence for 30-40 minutes at three, six, nine, and 12 months. **Components**: Behavioural counselling **Setting**: 2 community-based primary care practices. **Total duration**: 12 months. **Control Group**: multifactorial risk-factor counselling, during which the nurse practitioner explained the presence of unmodifiable risk factors, such as age, gender, and family history, and modifiable risk factors, such as lipid levels, diabetes mellitus, blood pressure, overweight, smoking habits, and physical activity.	
Outcomes	Medication adherence. Outcomes Measured at baseline & 3, 6, 9 months follow-up.	
Source of Funding	No records.	
Conflict of interest	None declared.	
Notes	Intervention group reported significantly higher levels of adherence to lipid lowering medication than patients in the control group.	
Risk of Bias		
Bias	**Authors' Judgment**	**Support for judgment**
Random Sequence Generation (Selection Bias)	Low risk	Randomisation schedules were developed from a computerized random-number generator, balanced at set intervals, using permutated blocks, to assure equal numbers in each group.
Allocation concealment (Selection Bias)	Low risk	Using sealed envelopes, patients were randomly assigned to either intervention or control group by the study statistician.
Blinding of participants and personal (performance bias)	Low risk	Neither the patient nor the research assistants delivering the motivational interviewing could be blinded to the intervention assignment due to the nature of the behavioural intervention.
Blinding of outcome assessment (detection bias)	Low risk	The clinic staff who recorded the BP data were blinded to patient assignment. The authors described that medication adherence data were downloaded automatically into the computer from the MEMS caps through a reader. Thus, both the RAs and patients could not affect MEMS adherence outcome.
Incomplete outcome data (Attrition bias)	Low risk	There were sufficient reporting of attrition, however 160 out of 190 patients (84%) were assessed based on returned MEMS pill caps, and 30 patients (16%) had no usable MEMS data due to damage. Of the 160 patients with MEMS data, 111 (70%) had complete. The Authors highlighted that the data were missing at random. A nonsignificant trend toward clinical outcome were appeared which may translate the effect of missing data.

Selective reporting (reporting bias)	Unclear risk	No protocol available although it appears that both primary and secondary outcomes (medication adherence and blood pressure (BP)) were reported, it is difficult to determine this without a protocol.
Group balance at baseline	Low risk	There were no significant differences between both groups at baseline, and their adherence rates were also similar.
Intention to treat analysis conducted	Low risk	Yes.
Groups receive same treatment (apart from the intervention)	Low risk	At baseline, the patients were assessed for demographics and clinical history. Follow-up assessments were conducted every 3 months and final assessment was conducted at 12 months. Both groups were completed all assessments at the same time intervals.

Rinfret et al. (2013)	
Methods	**Study design**: Randomised Controlled Trial **Country**: Canada **Dates patients recruited**: between June 2009 and June 2010 **Maximum follow-up**: 12 months
Participants	**Inclusion criteria**: Patients prescribed aspirin and clopidogrel (75 mg daily) **Exclusion criteria**: patients purchasing their medication in several different pharmacies, which would preclude adequate monitoring of drug adherence. **N randomised**: total: 300; intervention: 150; control: 150. **Diagnosis of Patients (% of pts):** patient with Acute Coronary Disease (ACS).
Interventions	**Intervention**: Intervention group received at hospital counselling on the importance of antiplatelet therapy. Nurse telephone calls within 7 days and at 1 month, 6 months and 9 months to assess adherence, reinforced optional drug compliance, and discuss medication nonadherence factors. **Components**: Behavioural counselling **Setting**: Tertiary care university cardiovascular centre and community. **Total duration**: 12 months. **Control Group**: received counselling before discharge as per usual clinical practice.
Outcomes	Medication adherence. Outcomes Measured at 1 week & 3, 6, 12 months follow-up.
Source of Funding	supported by an unrestricted research grant from BMS-Sanofi Canada
Conflict of interest	None declared.

Notes	The effect of the intervention on ASA or clopidogrel adherence remained largely unchanged.	
Risk of Bias		
Bias	**Authors' Judgment**	**Support for judgment**
Random Sequence Generation (Selection Bias)	Low risk	Using permuted blocks of 4, and 300 sealed envelopes with the patient number were prepared before recruitment
Allocation concealment (Selection Bias)	Low risk	Research assistants opened envelopes in sequence, after obtaining signed informed consent.
Blinding of participants and personal (performance bias)	High risk	No blinding, and the authors judge that as impractical.
Blinding of outcome assessment (detection bias)	Low risk	Two investigators were blinded as possible for collecting secondary outcomes by reviewing all study patient charts and angiographies without knowing the patient study group. All end points were adjudicated by one interventional cardiologist and one non-interventional cardiologist, blinded to the randomised group.
Incomplete outcome data (Attrition bias)	Low risk	A clear number of dropouts/ losses to follow-up were reported and the statistical plan was described. A 3 out of 150 patients who loss to follow-up required calculation adjustment that did not influence the results. Self-reported medication adherence was assessed at 6 and 12 months through phone calls, in a non-influential matter
Selective reporting (reporting bias)	Unclear risk	No protocol available, although it appears that everything was reported it is difficult to determine this without a protocol.
Group balance at baseline	Low risk	The Baseline social and clinical characteristics were well balanced for both groups.
Intention to treat analysis conducted	Low risk	Yes.
Groups receive same treatment (apart from the intervention)	Low risk	Both groups treated equally except for the intervention.

Schroeder et al. (2005)		
Methods	**Study design**: Randomised Controlled Trial **Country**: United Kingdom (UK) **Dates patients recruited**: from June–December 2001, following them up until December 2002 **Maximum follow-up**: 6 months	
Participants	**Inclusion criteria**: hypertension and who had a latest blood pressure recording of ≥ 150 mmHg systolic and/or 90 mmHg diastolic in the past six months. **Exclusion criteria**: Individuals who did not control their medication intake (such as some nursing home patients); secondary hypertension; severe dementia; other reasons for not approaching their patients such as recent bereavement. **N randomised**: total: 245; intervention: 128; control: 117. **Diagnosis of Patients (% of pts):** uncontrolled hypertension (100%)	
	Intervention: Nurse-led adherence support: consultation, practice nurses provided an adherence support session lasting for 20 minutes, followed by a shorter reinforcement session (10 minutes) two months later. During the consultation, practice nurses investigated whether patients understood their diagnosis and agreed with the treatment process. **Components**: education & Behavioural counselling **Setting**: General practices centres. **Total duration**: 18 months. **Control Group**: The control group received standard care delivered at their respective practices, apart from blood pressure checks at similar intervals as the participants in the intervention group.	
Outcomes	Adherence to medication. Outcomes Measured at 6 months follow-up.	
Source of Funding	Funded as part of a Medical Research Council Training Fellowship in Health Services Research (KS).	
Conflict of interest	None declared	
Notes	Both Intervention control groups reported high adherence to therapy.	
Risk of Bias		
Bias	**Authors' Judgment**	**Support for judgment**
Random Sequence Generation (Selection Bias)	Low risk	Patients were randomised using computer-generated random numbers
Allocation concealment (Selection Bias)	Low risk	The principal investigator passed the randomisation schedule on to the practice nurses shortly before the appointment for delivering the intervention. One author not involved in the rest of the study completed randomisation.
Blinding of participants and personal (performance bias)	High risk	Both the study participants and the practice nurses were aware of the group assignment at completion of the baseline period.

Blinding of outcome assessment (detection bias)	Low risk	Practice nurses were not involved in data collection and unaware of results until completion of the study although, they were aware of the group allocation.
Incomplete outcome data (Attrition bias)	Unclear risk	Six months: 10/120 missing from intervention groups (no reason given) and 18/112 missing from control group (1 unwell, 17 no reason given). Lost between groups not balanced. The authors stated that "due to data protection reasons, we were unable to obtain data on eligible participants who refused to take part, which would have allowed us to investigate any systematic differences between these individuals and the study participants".
Selective reporting (reporting bias)	Unclear risk	No protocol was found. The primary outcome was timing compliance of a single antihypertensive agent, however it is conceivable that timing compliance of all blood pressure lowering drugs was not as good as for the one that was observed compared to participants who were on more than one antihypertensive drug.
Group balance at baseline	High risk	Group were not similar at baseline in term of clinical characteristics (only 94 out of 245 participants (39%) were 'uncontrolled').
Intention to treat analysis conducted	Low risk	Yes.
Groups receive same treatment (apart from the intervention)	Low risk	The intervention groups received the Nurse-led adherence support except the control group received standard care delivered at their respective practices, apart from blood pressure checks at similar intervals as the participants in the intervention group.

Smith et al. (2008)	
Methods	**Study design**: Cluster Randomised Controlled Trial **Country**: United States **Dates patients recruited**: June 2004 to March 2005 **Maximum follow-up**: 9 months
Participants	**Inclusion criteria**: Patients diagnosis of MI, at least 18 years old and had a Beta-blocker prescription. **Exclusion criteria**: NR **N randomised**: total: 836; intervention: 426; control: 410. **Diagnosis of Patients (% of pts):** Myocardial Infarction (MI): (100%)

	Intervention: Simple direct-to patient intervention: two mailed communications: identical information about the importance of lifetime use of β-blockers following MI & that adverse effects can be managed & the importance of remembering to refill medication **Components**: education & Behavioural counselling **Setting**: Primary care centres. **Total duration**: 9 months. **Control Group**: NR	
Outcomes	Medication adherence. Outcomes Measured at 9 months follow-up.	
Source of Funding	By cooperative agreement from the Agency for Healthcare Research and Quality.	
Conflict of interest	None declared.	
Notes	A low-cost, easily replicable intervention can have an impact on patient's adherence to β-blocker therapy following MI.	
Risk of Bias		
Bias	**Authors' Judgment**	**Support for judgment**
Random Sequence Generation (Selection Bias)	Low risk	Patients randomly assigned to intervention or usual care by computer in sequential pairs (blocks of 2).
Allocation concealment (Selection Bias)	Low risk	Group assignment was concealed until allocation.
Blinding of participants and personal (performance bias)	Unclear risk	Blinding processes was not described. No description of who was or was not blinded.
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessment was blinded.
Incomplete outcome data (Attrition bias)	Low risk	Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups (figure 1).
Selective reporting (reporting bias)	Unclear risk	No protocol available.
Group balance at baseline	Low risk	Patients in the intervention arm and those in the control arm were similar in terms of demographic and clinical characteristics.
Intention to treat analysis conducted	Low risk	Yes.
Groups receive same treatment (apart from the intervention)	unclear risk	There was no intervention description for Control group to compare with the intervention group.

Wald et al. (2014)		
Methods	**Study design**: Randomised Controlled Trial **Country**: United Kingdom (UK) **Dates patients recruited**: Between February 2012 and August 2013 **Maximum follow-up**: 6 months	
Participants	**Inclusion criteria**: Patients must owned a mobile telephone with text message capability and who had been prescribed blood pressure and/or lipid-lowering medication. **Exclusion criteria**: NR **N randomised**: total: 303; intervention: 151; control: 152. **Diagnosis of Patients (% of pts):** cardiovascular disease.	
	Intervention: Text Messaging Intervention (TM): a 2 way automatic generated TM sent daily for two weeks, then alternate day texts for two weeks & then weekly texts for 22 weeks (6 months overall). **Components**: education & Behavioural counselling **Setting**: Primary care centres. **Total duration**: 24 months. **Control Group**: not receive text messages.	
Outcomes	Medication adherence. Outcomes Measured at 6 months follow-up.	
Source of Funding	Supported by Astra Zeneca, Barts Hospital Special Trustees and Queen Mary Innovation.	
Conflict of interest	None declared.	
Notes	Text messaging improved medication adherence compared with no text messaging.	
Risk of Bias		
Bias	**Authors' Judgment**	**Support for judgment**
Random Sequence Generation (Selection Bias)	Low risk	Patients were randomised using computer generated in blocks of 4 and allocated centrally from the coordinating centre by telephone
Allocation concealment (Selection Bias)	Unclear risk	Allocation concealment was not described.
Blinding of participants and personal (performance bias)	High risk	Blinding processes was not described. No description of who was or was not blinded.
Blinding of outcome assessment (detection bias)	High risk	Blinding processes was not described.

Incomplete outcome data (Attrition bias)	Unclear risk	Dropouts were equal across groups (one patient in each group). Reasons for dropout were not given.
Selective reporting (reporting bias)	Low risk	The study protocol was provided and all the primary and the secondary outcomes were presented before and after the intervention.
Group balance at baseline	Low risk	The baseline characteristics of the two randomised groups were similar.
Intention to treat analysis conducted	High risk	No.
Groups receive same treatment (apart from the intervention)	Low risk	Both groups received the same treatment except intervention.

Appendix B Characteristics of Studies by Type of Intervention

Supplemental File 2

Table S2: Characteristics of studies by type of medication adherence intervention

Author(s) & year	Intervention	Outcomes Assessment Methods	Medication Adherence Measures	Key findings
Ho et al. (2014) USA	Multifaceted Intervention: 1) Medication reconciliation & tailoring: 2) Patient Education about medications: 3) Collaborative care: 4) Voice messaging for medication reminder & medication refill calls	■ Intention to treat, Appropriate descriptive statistics to summarize baseline traits, Un-paired t tests, $\chi 2$ tests, Log-rank test, Wilcoxon rank sum test & Sensitivity analysis	Pharmacy refill data for 4 cardiac medications (based on a mean proportion of days covered (PDC)/ 365 days follow-up	■ **IG**: 89.3% were adherent compared with 73.9% of **CG** patients (95% CI: 15% (5 to 26), NNT = 6.7, *P* = .003) for 4 classes of medications & the mean PDC (0.94 v 0.87; *P* < .001). Wilcoxon rank sum test used to compare proportion of days covered (PDCs) between study arms. ■ There was a greater BP control, decline in systolic BP (−12 v −4mmhg) & decline in diastolic BP (−5 v −3mm hg) for intervention patients
Leiva et al. (2014) Spain	Brief Multifactorial adherence-based intervention: motivational interviewing, pillbox reminders, family support, BP measurements & antihypertensive reminder forms, & simplification of dosing regime	■ Intention-to-treat basis, Fisher's exact test & the chi-squared tests, Student's t-test, means of a generalized linear model, Relative risks (RR), & the absolute risk reduction and number needed to treat	Medication refills data based on the medication possession ratio (number of days supply of medication dispensed divided by the number of days' evaluated	■ No significant difference in adherence to anti-hypertensive medication observed at 12 months between groups (76%, 75.3% in **IG**, & 76.7% in CG; & 51.4% in IG versus 50.8% in **CG;** *p* < 0.789**)**. Means of a generalised linear model was used to assess the effect of intervention.
Author(s) & year	**Intervention**	**Outcomes Assessment Methods**	**Medication Adherence Measures**	**Key findings**
Kripalani et al. (2012) USA	Graphically Enhanced Interventions: 4 groups: 1) patients received usual care, 2) refill reminder postcards, 3) illustrated daily medication schedules, or 4) both interventions for one year after completed a 30–45 minute interviewer assisted questionnaire	■ Descriptive statistics, ANOVA, Chi-square, Logistic regression, Post-hoc	Self Efficacy Appropriate Medication Use Scale (SEAMS) 4-item Morisky Medication Adherence Scale (MMAS)	■ Illustrated medication schedule group had greater odds of adherence (OR = 2.2; 95 % CI, 1.21 to 4.04, *P* = 0.010) but also low self-efficacy for managing medications (OR = 2.15; 95 % CI, 1.11 to 4.16; *P* = 0.023). ■ At 1-year follow-up, no statistically difference in adherence rate between groups (32.9 % vs.32.9 respectively, *P* = 1.0) of refill reminder postcards

				■ Overall, refill reminder postcards group did not have better adherence (OR = 1.01; 95 % CI, 0.67 to 1.52). Chi-square test was used to determine the effect of treatment assignment on the primary outcome.
Smith et al. (2008) USA	Simple direct-to patient intervention: 2 mailed communications: identical information about the importance of lifetime use of β-blockers following MI & that adverse effects can be managed & the importance of remembering to refill medication	■Growth curve (multilevel) analysis, number of patients needed to treat &the resulting odds ratio was corrected to be interpreted as a relative risk (RR) because 80% PDC occurred more than 10% of the time in the sample, intention-to-treat analysis.	Proportion of Days Covered (**PDC**) per month	■ **IG** had absolute increased by 4.3% of days covered per month compared to 3.7% in **CG** (5.7% relative change from baseline) which represent (*P* =.04 ■ **IG** were 17% more likely to have a PDC of 80%, (Relative Risk = 1.17; 95% CI = 1.02 to1.29; *P* = 0.04) or greater over the entire post-intervention period ■ At baseline, PDC did not differ between groups (IG: 87%; CG: 86%). Growth curve (multilevel) analysis was used to evaluate the effect of intervention on adherence.
Wald et al. (2014) UK	Text Messaging Intervention (TM): a 2-way automatic generated TM sent daily for two weeks, then alternate day texts for two weeks & then weekly texts for 22 weeks (6 months overall)	■ Chi-squared tests, t-tests, Wilcoxon rank-sum tests, 95% Confidence Intervals, Subgroup analyses on the use of medication & interaction tests were performed	Electronic prescription records: determined medication use by personal enquiry at clinic visit by calculating the number of days' medication taken in 28 days	■ 16% improvement in medication adherence (95% CI 7–24%, *P* <0.001) at 6 months for patients' who took medication on <22 days of the last 28 days following-up in both groups. ■ There was a statistically significant difference between groups 9% (3–14%, *P* = 0.002) & 7% (0.2–14%, *P* = 0.045), respectively in % of patients who stopped medication completely & continued to take <80% of the prescribed regime. Interaction tests were performed on the basis of a significant level of 0.01 or less.

Author(s) & year	**Intervention**	**Outcomes Assessment Methods**	**Medication Adherence Measures**	**Key findings**
Hacihasanoğlu & Goözuöm (2011) Turkey	Nurse-based educational intervention & in-home monitoring for medication adherence: three groups A, B, & CG. Groups A & B received a total of six-monthly education sessions about medication adherence. Group B also received individual & structured educational phone call about healthy lifestyle behaviours.	■ Chi-square & variance analysis (ANOVA), Paired t-test, Variance analysis, Turkey, McNemar test, & a significance level of p = 0.05 were used	Medication Adherence Self-Efficacy Scale (MASES)	■ At baseline, no statistically significant differences between all groups for medication adherence self-efficacy in the mean score pre-test (55.30 (SD = 7.57); 55.55 (SD = 7.67); 55.12 (SD = 8.53) respectively, T value = 0 .029 *P* = 0 .971 ■ At 10 months, significant increase in medication intake ratios in both group A&B (80%, 85%), respectively, *P*≤ 0.001) compare to CG (42%), *P*> 0.05). ■ Combined education (Group B) was more effective than medication adherence education alone (Group A) on adherence self-efficacy (71.10 (SD = 6.42); 72.27 (SD = 5.27); 56.85 (SD = 6.10) respectively, T value = 83 .131; *p* ≤ 0.001. Paired t-test & Variance analysis were used for inter-group assessment of significance of the differences

				between the average pretest and posttest scores of medication adherence.
(Rinfret et al. 2013) Canada	IG received at hospital counselling on the importance of antiplatelet therapy. Nurse telephone calls within 7 days and at 1 month, 6 months and 9 months to assess adherence, reinforced optional drug compliance, discuss medication nonadherence factors	■ Two-way analysis of variance, intent-to-treat, survival statistical methods with the log-rank test, Fisher exact test, linear regression	Pharmacy refill data of aspirin & clopidogrel	■ At 12 months, median refill-adherence scores was in higher rate for aspirin & clopidogrel 99.2% (97.5–100%) and 99.3% (97.5–100%) respectively in IG vs. 90.2% (84.2–95.4%) & 91.5% (85.1–96.0%) respectively, in the CG, $P = 0.0001$. ■ At 12 months, 87.2% of IG reported persistence taking clopidogrel vs 43.1% in CG ($P < 0.0001$). Two-way analysis of variance and Wilcoxon-Mann-Whitney tow-sided test were used for all primary and secondary medication adherence end points.

Author(s) & year	**Intervention**	**Outcomes Assessment Methods**	**Medication Adherence Measures**	**Key findings**
Ma et al. (2014) China	Motivational interview Counselling based on Social Cognitive Theory (SCT)	■ Skewness & Kurtosis test, Descriptive statistical analyses, the independent samples t-test, & the paired samples t-test analysis.	Treatment Adherence Questionnaire of Patients with Hypertension (TAQPH)	■ MI group showed increased in mean ±SD adherence in medication treatment between the baseline vs. post-intervention (23.25 (SD = 3.02) & 29.72 (SD = 3.46) respectively t value = 0.039, $P = 0.034$ ■ The mean scores for medication adherence were increase within-group differences in the IG & CG at baseline and six months of 23.25 (SD = 3.02); 29.72 (SD = 3.46), t value = 0.039, $P = 0.034$) & 22.13 (SD = 2.89); 25.30 (SD = 3.11), t value = 0.039, $P = 0.061$), respectively. ■ A significant drop in DPS BP values for the MI group 89.01mmHg (SD = 14.72) & 82.55 (SD = 15.18), t value = 0.027, $P = 0.036$ respectively. The independent samples t-test was used to examine the difference between MI group & usual care group.
Ogedegbe et al. (2008) USA	Motivational interviewing (MINT) for improving medication adherence: MINT group received behavioural counselling about medication adherence for 30-40 minutes at three, six, nine, and 12 months.	■ Intention-To-Treat principle, mixed-effect regression models, sensitivity analyses, & Little's MCAR test were used	Medication Event Monitoring System (MEMS) Self-reported Morisky Medication Adherence Scale (MMAS-8)	■ At baseline, medication adherence was similar in both groups (56.2% and 56.6% for MINT & CG, respectively, $P = 0.94$). ■MINT group had a higher MEMS adherence rate compared to CG (57% vs. 43%, respectively, $P = 0.027$), with absolute difference of 14% (95% CI, −0.2 to –27%). ■ MINT group had a slight increase between the baseline vs. post-intervention adherence rate (1.1%, t = .24 with 159 df, $P = 0.810$) compared to (−12.9%, t = −2.89 with 159 df, $P = 0.004$) in CG. Mixed-effect regression models was used to test the time X group interaction.

Author(s) & year	Intervention	Outcomes Assessment Methods	Medication Adherence Measures	Key findings
Beune et al. (2014) Netherlands	Nurse-led Culturally Adapted Hypertension Education (**CAHE**): three structured 30 minute culturally appropriate counselling sessions at 2 weeks, 8 weeks & at 20 weeks, and then written educational materials.	■ Intention-to-treat analysis, logistic regression analysis, linear regression analysis were used	Self-reported Morisky Medication Adherence Scale (MMAS-8)	■ A small increase in medication adherence occurred in both groups (0.51, 95% CI: 0.03 to 1.04, $p = 0.672$ vs. 0.65, 95% CI: 0.19 to 1.12, $p = 649$) from baseline (5.59) to follow-up assessment (6.24) in the CG. ■ No significant difference between groups for self-reported medication adherence after adjustment (–0.09, –0.65 to 0.46; $P = 0.74$). The analyses was based on the logistic regression analysis.
Guirado et al. (2011) Spain	Nurse-led counselling & education	■ Intention-to-treat basis, statistical tests for independent data, & tests for related data.	Haynes-Sackett and Morisky-Green tests	■ No statistically significant differences between the IG and CG groups following the intervention at 12 months follow-up IG: 9.6% (5.5% to 13.6%); CG: 8.8% (4.9% to 12.6%).
Jiang et al. (2007) China	Nurse-led cardiac rehabilitation program	■ Intention-to-treat basis & Mann-Whitney U-test, t-test or Chi-square test, the normality test of the data & were used	Self-Reported Drug Compliance Scale	■ IG had a better medication adherence from baseline 4.85 (SD = 0.35) to statistically significant level of 4.70 (SD = 0.51) at 3 months with a net change of –0.15 (0.63); U test = –2.17, $P < 0.05$ ■ At 6 months, IG had a mean score of medication adherence of 4.47 (SD = 0.62) with a net change –0.38 (SD = 0.69), *U* test = –1.46, $P < 0.143$. Mann-Whitney U-test, t-test or Chi-square test, the normality test of the data & were used to test the differences between the IG & CG.
Nieuwkerk et al. (2012) Netherlands	Nurse-led multifactorial cardio-vascular risk-factor counselling: focused on changing modifiable risk factors such as increasing medication adherence	■ Intention to treat, repeated-measures linear mixed models, Generalized estimating equations, Linear mixed model, & Persons correlation coefficients were applied.	Self-Reported Questionnaire & Beliefs about Medication Questionnaire (BMQ)	■ At 18 months, both IG & CG had higher level of adherence to lipid lowering medication (95% to 100% vs. 90% to 95%) respectively. ■ At 18 months follow-up, IG had higher adherence to statins therapy than CG (9.39 (SD = 0.15) vs. 8.86 (D = 0.15) respectively, with an absolute difference of 0.53 (0.02–1.05), ($r = –0.36$, $P < 0.01$). Linear mixed model was used to investigate differences between the 2 groups in adherence to medication.
Schroeder et al. (2005) UK	Nurse-led adherence support: consultation, practice nurses provided an adherence support session lasting for 20 minutes,	■ Descriptive Statistics, intention-to-treat analysis, Multivariable regression models, pre-planned subgroup	Electronic Medication Monitor System (MEMS)	■ At baseline, IG had a high adherence 90.8 (SD = 15.6%) & similar to **C**G: 94.5 (SD = 7.6%), ($P = 0.63$).

followed by a shorter reinforcement session (10 minutes) two months later.	analyses & simple one-way sensitivity analysis	■ At six months, no difference in adherence rate between IG & CG (adjust difference in mean–1.0%; 95% CI –5.1 to 3.1). Multivariable regression models were used to compare the intervention effect.

Abbreviations: **IG**: intervention group, **CG**: control group, **PDC**: proportion of days covered, ***P***: p value, **F** = frequency, **MMAS-8:** self-reported Morisky medication adherence scale-8 items, **MEMS**: electronic medication monitor system, **BMQ**: belief about medication questionnaire, **MASES:** medication adherence self-efficacy scale, OR: odds ratio, **MINT**: motivational interviewing, **SD**: standard deviation.

Appendix C University of Technology Sydney (UTS) Human Research Ethics Committee Approval

UTS
UNIVERSITY OF TECHNOLOGY, SYDNEY

Dear Applicant

[External Ratification: 1. SESLHD HREC 2. SESLHD Research Support Office – 1. HREC 16-085 (HREC/16/POWH/218) 2. SSA 16/G/103– 08/06/2016 to 08/06/2021]

The UTS Human Research Ethics Expedited Review Committee has reviewed your application titled, "Behaviour Change Interventions to Improve Medication Adherence in Patients with Cardiac Disease", and agreed that the application meets the requirements of the NHMRC National Statement on Ethical Conduct In Human Research (2007). **I am pleased to inform you that your external ethics approval has been ratified.**

Your approval number is **UTS HREC REF NO. ETH16-0635**.

Approval will be for the period specified above and subject to the provision of annual reports and evidence of continued support from the above-named Committee.

Please note that the ethical conduct of research is an on-going process. The National Statement on Ethical Conduct in Research Involving Humans requires us to obtain a report about the progress of the research, and in particular about any changes to the research which may have ethical implications. This report form must be completed at least annually, and at the end of the project (if it takes more than a year). The Ethics Secretariat will contact you when it is time to complete your first report.

I also refer you to the AVCC guidelines relating to the storage of data, which require that data be kept for a minimum of 5 years after publication of research. However, in NSW, longer retention requirements are required for research on human subjects with potential long-term effects, research with long-term environmental effects, or research considered of national or international significance, importance, or controversy. If the data from this research project falls into one of these categories, contact University Records for advice on long-term retention.

You should consider this your official letter of approval. If you require a hardcopy please contact Research.Ethics@uts.edu.au.

To access this application, please follow the URLs below:

* if accessing within the UTS network:
* if accessing outside of UTS network: , and click on " RM6 – Production" after logging in.

We value your feedback on the online ethics process. If you would like to provide feedback please go to:

If you have any queries about your ethics approval, or require any amendments to your research in the future, please do not hesitate to contact Research.Ethics@uts.edu.au.

Yours sincerely,

Professor Marion Haas
Chairperson
UTS Human Research Ethics Committee
C/- Research & Innovation Office
University of Technology, Sydney
E:

Appendix D Human Research Ethics Committee Approval- Prince of Wales Hospital (POWH)

Health
South Eastern Sydney
Local Health District

HUMAN RESEARCH ETHICS COMMITTEE
Room G71 East Wing
Edmund Blacket Building
Prince of Wales Hospital
RANDWICK NSW 2031
Tel: 02 9382 3587 Fax: 02 9382 2813
RSOSESLHD@SESIAHS.HEALTH.NSW.GOV.AU
www.seslhd.health.nsw.gov.au/POWH/researchsupport

08 June 2016

Mr Ali Al-Ganmi
Faculty of Health
University of Technology Sydney
PO Box 123
Broadway NSW 2007

Dear Mr Al-Ganmi

HREC ref no: **16/085 (HREC/16/POWH/218)**
Project title: **Behaviour Change Interventions to Improve Medication Adherence in Patients with Cardiac Disease**

Thank you for submitting the above application for ethical and scientific review, and for your correspondence dated **31.05.2016** to the Executive Officer responding to questions which arose at the HREC meeting on **26 April 2016.**

Authority to grant final approval was delegated to the Executive Officer and I am pleased to advise that ethical approval has been given for the following:

- NEAF submission code AU/1/C4C4214, dated 14 March 2016
- Protocol, version 2, dated 20 May 2016
- Participant Information Sheet (Survey and Interview Phase) Version 2, 20/05/2016
- Participant Information Sheet (Pilot Trial Phase) Version 2, 20/05/2016
- Survey: Version 1: 14/03/2016
- An Example of a Motivational Interviewing for a Standard Cardiac Patient: Version (1) 14.03.2016
- Semi-Structured Interview: Version (1) 14.03.2016
- The text message (TM) reminder content: version (1) 14.03.2016
- The Experimental Intervention, not dated

Ethical approval is valid for the following site(s):

- Prince of Wales Hospital

Conditions of approval

Prince of Wales Hospital
Community Health Services
Barker Street
Randwick NSW 2031

Appendix E Participants Information Sheet and Consent Form

University of Technology Sydney (UTS)

Prince of Wales Hospital (POWH)

PARTICIPANT INFORMATION SHEET

Behaviour Change Interventions to Improve Medication Adherence in Patients with Cardiac Disease: Survey and Interview

Invitation

You are invited to participate in a PhD research project being undertaken by Ali Al-Ganmi (a nursing doctoral student at University of Technology Sydney (UTS), and supervised by Professor Lin Perry (Prince of Wales Hospital and UTS) and Dr. Leila Gholizadeh (UTS).

Please read this information sheet carefully and make sure that you understand its contents before deciding to participate.

We are asking for your help in a study that looks at how cardiac patients manage their cardiac medications. We are undertaking this study because reports show that a lot of people do not take their medicines as prescribed. On average only about half of medicines are taken as prescribed and this is a risk for people’s health. We are interested in identifying strategies that could help people take their medications as prescribed.

Before you decide whether or not you wish to take part in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. If you have further questions about the research project, please feel free to contact the primary researcher, Ali Al-Ganmi or one of his supervisors using the contact details provided.

1. What is the purpose of this study?

The purpose of this study is to identify those factors that influence patients' willingness and ability to take their heart medicines as prescribed. We hope to use this information to help us provide better support for patients as they attempt to manage their medications.

2. Why have I been invited to participate in this study?

You are eligible to take part in this study because you are an adult referred for cardiac rehabilitation who takes at least one heart medicine.

3. What if I don't want to take part in this study, or if I want to withdraw later?

Participation in this study is voluntary. It is completely up to you whether you wish to take part or not. If you decide not to take part, it will not affect your care at this hospital now or in the future. Whatever your decision, it will not affect your relationship with the staff caring for you.

If you wish to withdraw from the study once it has started, you can do so at any time without having to give a reason.

4. What does this study involve?

If you agree to take part in this first part of the study, you will be asked to sign the Participant Consent Form.

If you wish to take part in this part of the study you will first be asked to answer some survey questions about how you take your heart medicines and how you feel about taking medicines under different situations, and what factors affect how you take your medications. The survey will also ask some questions about you. The paper-based questionnaire will be given to you when you attend for cardiac rehabilitation, and you will be encouraged to complete it whilst you are at the hospital and to place the completed questionnaire in a box in the cardiac rehab gym after your session. However, if you prefer, you can complete the questionnaire at home and post it back via mail using the enclosed prepaid envelope.

Next, you will be asked if you would like to be interviewed to discuss your experiences with your medications with the researcher in more detail. This will take about 30-45 minutes, talking to the researcher about your medications and things that affect how you take them. This interview will be audio-recorded, so no details are missed. At the end of your interview, based on the result of your answers to the questionnaire and your interview, you may be invited to participate in phase 3 of the study.

The analysis is focused on patient groups rather than on individuals. All responses will be kept confidential. Your doctors and healthcare providers will not know whether you took part or what you said.

Your information will be identified by a code number only. No-one other than the research team will who took part.

There are no adverse consequences to you if you decide not to take part. If you do decide to take part, you will be given this information sheet to keep and asked to sign the study consent form.

You are free to withdraw from the study at any time without having to give a reason**.**

5. How is this study being paid for?

- No one is being paid for this study.

6. Are there risks to me in taking part in this study?

There is no foreseeable risk for participating in this study. However, it is possible that some people may feel uncomfortable in sharing personal information or reasons for not taking medicines as prescribed.

The researcher will not divulge information you share without your consent. If the information you give about how you take your medicines suggests your health is at risk because of the way you are taking the heart medicines prescribed for you, the researcher will advise that you seek further information and help from your General Practitioner.

7. What are the alternatives to participation?

Whether or not you participate in this study you are eligible to attend the routine cardiac rehabilitation program you have been referred to.

8. What happens if I suffer injury or complications as a result of the study?

If you suffer any injuries or complications as a result of this study, you may have a right to take legal action to obtain compensation for any injuries or complications resulting from the study.

Compensation may be available if your injury or complication is caused by the negligence of one of the parties involved in the study. If you receive compensation that includes an amount for medical expenses, you will be required to pay for your medical treatment from those compensation monies. You do not give up any legal rights to compensation by participating in this study.

If you are not eligible for compensation for your injury or complication under the law, but are eligible for Medicare, then you can receive any medical treatment required for your injury or complication free of charge as a public patient in any Australian public hospital.

9. Will I benefit from the study?

- There is no financial benefit for taking part in this study.
- Taking part in this study may help you better understand your heart medications and their importance.
- You may learn better ways of taking your medication;
- Other people like you may benefit in the future from the results of this study.
- The information from this study may help nurses provide better care for future patients; however this study may not directly benefit you.
- You will receive usual care in the cardiac rehabilitation programme, whether or not you take part in this study.

10. Will taking part in this study cost me anything, and will I be paid?

- Participation in this study will not cost you anything other than the cost of replying to the text messages and you will not be paid.

11. How will my confidentiality be protected?

None of the healthcare staff will know whether or not you are taking part in this study. Only the research team will know who is taking part in this study. All identifiable information collected about you in connection with this study will remain confidential and will be disclosed only with your permission, or except as required by law. Only the study researchers, named above will have access to the information you provide and the information will be kept secure at the University of Technology Sydney (UTS).

12. What happens with the results?

If you give us your permission by signing the consent document, we plan to discuss/publish the results in local and international peer-reviewed nursing journals, in national and international conferences and in an online thesis. In any publication, information will be provided in such a way that you cannot be identified. Results of the study will be also provided to you, if you wish.

13. What should I do if I want to discuss this study further before I decide?

When you have read this information, the researcher Ali Al-Ganmi, will discuss the study further with you and answer any queries you may have. If you would like to know more at any stage, please do not hesitate to contact him on [redacted].

14. Who should I contact if I have concerns about the conduct of this study?

This study has been approved by the South Eastern Sydney Local Health District Human Research Ethics Committee. Any person with concerns or complaints about the conduct of this study should contact the Research Support Office which is nominated to receive complaints from research participants. You should contact them on 02 9382 3587, or email and quote [*HREC project number*].

Also, if you have any complaints about the ethical conduct of this research, you may contact the Ethics Committee through the Research Ethics Office at University of Technology Sydney, City campus, 15 Broadway Ultimo NSW 2007, T +61 2 9514 2000 or email; During this study, Ali Al-Ganmi is supervised by Professor Lin Perry and Dr. Leila Gholizadeh, Faculty of Health, University of Technology, Sydney. You may contact these people if you have any concerns about the way the study is conducted:

Principal Researcher: Mr Ali Al-Ganmi: T. ([redacted]).

Research Supervisor: Professor Lin Perry M. (+61[redacted]), T. (+61 [redacted]).

Research Co-supervisor: Dr. Leila Gholizadeh: T. (+61 2 95144814).

Thank you for taking the time to consider this study.

If you wish to take part in it, please sign the attached consent form.

This information sheet is for you to keep.

University of Technology Sydney (UTS)

Prince of Wales Hospital (POWH)

CONSENT FORM: Survey and Interview

Behaviour Change Interventions to Improve Medication Adherence in Patients with Cardiac Disease: Survey and Interview

1. I,...
   of..
   agree to participate in the study described in the participant information statement ***attached to this form.***

2. I acknowledge that I have read the participant information statement, which explains why I have been selected, the aims of the study and the nature and the possible risks of the investigation, and the statement has been explained to me to my satisfaction.

3. Before signing this consent form, I have been given the opportunity of asking any questions relating to any possible physical and mental harm I might suffer as a result of my participation and I have received satisfactory answers.

4. I understand that I can withdraw from the study at any time without prejudice to my relationship to the researchers from the University of Technology, Sydney and the Prince of Wales Hospital.

5. I agree that research data gathered from the results of the study may be published, provided that I cannot be identified.

6. I understand that if I have any questions relating to my participation in this research, I may contact the SESLHD Human Research Ethics Committee, South Eastern Sydney Local Health District, Prince of Wales Hospital, Randwick NSW 2031 on telephone

   02-9382 3587, who will be happy to answer them.

7. I acknowledge receipt of a copy of this Consent Form and the Participant Information Statement.

Complaints may be directed to the Research Ethics Secretariat, South Eastern Sydney Local Health District, Prince of Wales Hospital, Randwick NSW 2031 Australia (phone 02-9382 3587, fax 02-9382 2813, email .

Signature of participant	**Please PRINT name** **[or person responsible]**	**Date**
______________________	______________________	____________
Signature of witness	**Please PRINT name**	**Date**
______________________	______________________	____________
Signature of investigator	**Please PRINT name**	**Date**
______________________	______________________	____________

University of Technology Sydney (UTS)

Prince of Wales Hospital (POWH)

Behaviour Change Interventions to Improve Medication Adherence in Patients with Cardiac Disease

WITHDRAWAL OF CONSENT

I hereby wish to **WITHDRAW** my consent to participate in the study described above and understand that such withdrawal **WILL NOT** jeopardise any treatment or my relationship with the (*University of Technology Sydney, Prince of Wales Hospital or my medical attendants)*.

Signature of participant	**Please PRINT name**	**Date**
[or person responsible]		
____________________	______________________	_______________

The section for Revocation of Consent should be forwarded to **Mr. Ali Al-Ganmi, c/o Prof Lin Perry, G74, East Wing Edmund Blacket Building, Prince of Wales Hospital, Randwick, NSW 2031.**

M.: [redacted]. Email: ali.h.al-ganmi@student.uts.edu.au.

Appendix F Socio-Demographic Data Sheet and Medication Adherence Questionnaires

University of Technology Sydney (UTS)

UNIVERSITY OF TECHNOLOGY SYDNEY

THE PRINCE OF WALES HOSPITAL

Prince of Wales Hospital (POWH)

Survey

Study title: Behaviour Change Interventions to Improve Medication Adherence in Patients with Cardiac Disease: Survey

Situations come up that make it difficult for people to take their medicines as prescribed by their doctors. Below is a list of such situations. We want to know your opinion about taking your cardiac medicine(s) under each of them.

Please indicate your response by putting across in the box that most closely represents your opinion.

	Yes	No
1. Do you ever forget to take your medicine?		
2. Are you careless at times about taking your medicine?		
3. When you feel better do you sometimes stop taking your medicine?		
4. Sometimes if you feel worse when you take your medicine, do you stop taking it?		

Please put a cross in the box that is closest to your opinion.

	None of the time	**Some of the time**	**Most the time**	**All the time**
5. How often do you forget to take your medicine				
6. How often do you decide not to take your medicine?				
7. How often do you forget to get prescriptions filled				
8. How often do you run out of medicine?				
9. How often do you skip a dose of your medicine before you go to the doctor?				
10. How often do you miss taking your medicine when you feel better?				
11. How often do you miss taking your medicine when you feel sick?				
12. How often do you miss taking your medicine when you are careless?				
13. How often do you change the dose of your medicines to suit your needs (like when you take more or less pill than you're supposed to)?				
14. How often do you forget to take your medicine when you are supposed to take it more than once a day?				
15. How often do you put off refilling your medicines because they cost too much money?				
16. How often do you plan ahead and refill your medicines before they run out?				

There are no right or wrong answers. For each of the situations listed below, please rate how sure you are that you can take your cardiac medicines all of the time.

How confident are you that you can take your cardiac medications?	**Not at all sure**	**A little sure**	**Fairly sure**	**Extremely sure**
17. When you're busy at home				
18. When there is no one to remind you				
19. When you worry about taking them for the rest of your life				
20. When you do not have any symptoms				
21. When you are with family members				
22. When you are in a public place				
23. When the time to take them is between your meals				
24. When you are travelling				
25. When you take them more than once a day				
26. When you have other medications to take				
27. When you feel well				
28. If they make you want to urinate while away from home				
Please rate how sure you are that you can carry out the following task:				
29. Make taking your medicines part of your routine				

There are no right or wrong answers. For each of the statements listed below, please rate whether you agree or disagree.

	Strongly Agree	**Agree**	**Uncertain**	**Disagree**	**Strongly Disagree**
30. My health, at present, depends on my medicines					
31. My medicines protect me from becoming worse					
32. My medicines disrupt my life					
33. I sometimes worry about long-term effects of my medicines					
34. Doctors use too many medicines					
35. People who take medicines should stop their treatment for a while every now and again					
36. Most medicines are addictive					
37. Medicines do more harm than good					

For these last questions, please indicate how often people may have helped you during the PAST THREE MONTHS.

How often has someone in the past three months -?

	Never	**Rarely**	**Sometimes**	**Often**	**Very often**
38. Helped you monitor your symptoms and medicines side effects?					
39. Reminded you to take your medicines?					
40. Picked up your cardiac medicines prescriptions for you?					
41. Helped you understand information about your medicines?					
42. Checked in with you about your medicines?					
43. Encouraged you to talk to your doctor about your medicines when you have questions or problems?					
44. Helped you to believe you can take your medicines as prescribed?					
45. Called you specifically to ask how you were doing with your cardiac medicines?					

University of Technology Sydney (UTS)

UNIVERSITY OF TECHNOLOGY SYDNEY

Prince of Wales Hospital (POWH)

THE PRINCE OF WALES HOSPITAL

Data Collection Sheet

Please can you give a few details about yourself and your REGULAR medicines.
Please put a cross against the answer that is closest for you

1. Age: _________ years **2. Gender**: Male ☐ Female ☐

DEMOGRAPHIC DETAILS: (Patient Questions)

Please put a cross against your closest response:

3. Employment Status:

Employed ☐ Unemployed ☐ Retired ☐

4. Living Arrangement:

Lives alone ☐ Live with spouse/ partner ☐ Live with others ☐

5. Marital Status:

Married/De fecto ☐ Widowed/Divorced ☐ Single ☐ Separated ☐

6. Ethnicity/Country of birth Australian/New Zealand ☐ Others ☐

7. Education: years of full time education completed ---------------------------- years

Diseases you have been diagnosed with (Put a X in the box for those that apply to you):

8. Medical condition

Co-morbidities Yes ☐ No ☐ Diabetes Mellitus Yes ☐ No ☐

9. Finally, please can you give a few details about your REGULAR medicines Do you remember your heart medications and the number you take per day for every medication?

Please list:

Cardiac medications:

Drug 1: Name ____

Dosage per day (if known)___________________________________

Number of pills taken: _______________Number of times per day_____

Drug 2: Name ____

Dosage per day (if known)___________________________________

Number of pills taken: _______________Number of times per day_____

Drug 3: Name ____

Dosage per day (if known)___________________________________

Number of pills taken: _______________Number of times per day_____

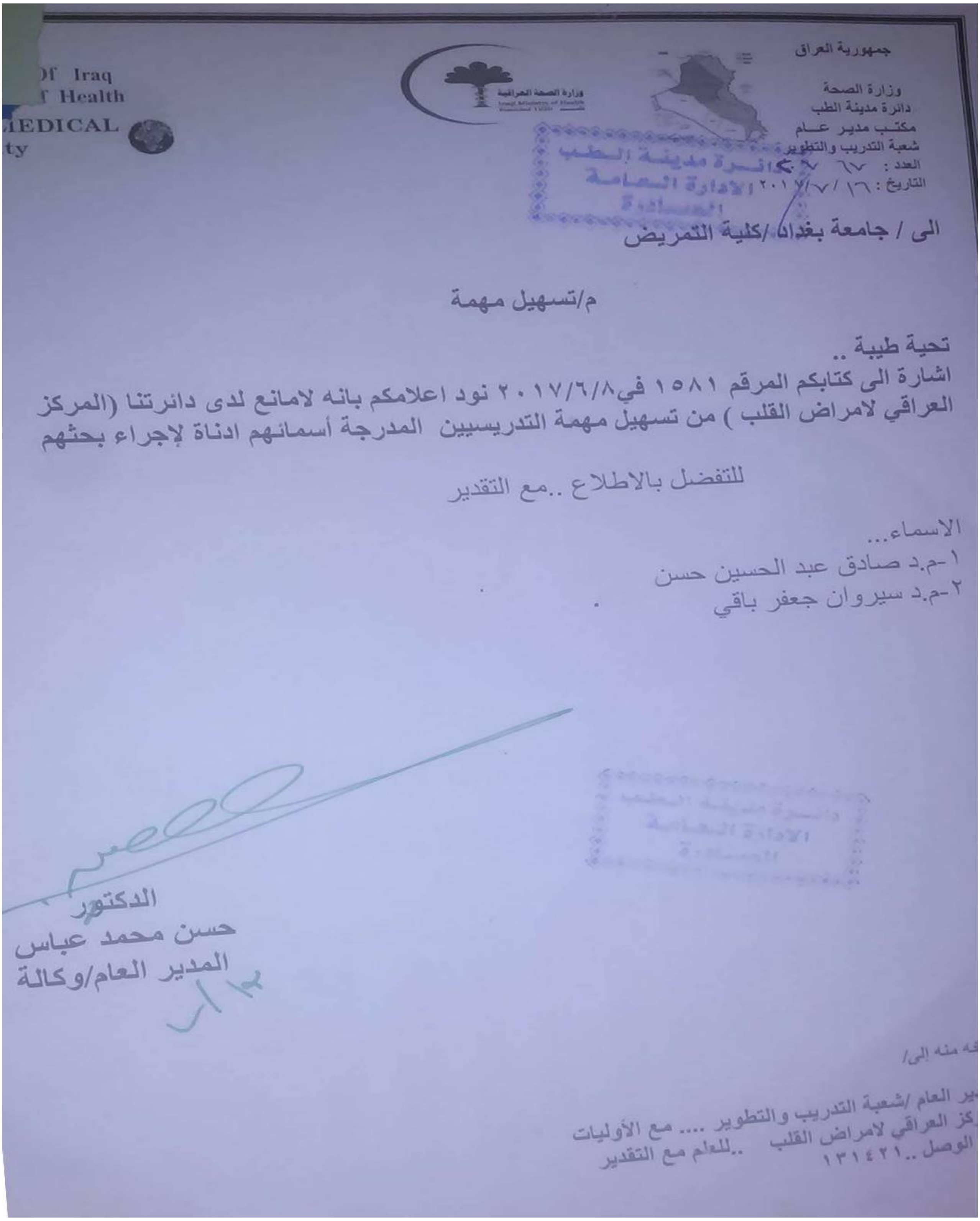
Drug 4: Name ____

Dosage per day (if known)___________________________________

Number of pills taken: _______________Number of times per day_____

Continue overleaf if needed, THANK YOU FOR COMPLETING THIS

Appendix G Iraqi Hospitals Health District Human Research Ethics Committees Approval



...Of Iraq
...f Health
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جمهورية العراق
وزارة الصحة
دائرة مدينة الطب
مكتب مدير عـام
شعبة التدريب والتطوير
العدد : ٦٧
التاريخ : ١٦ / ٧ / ٢٠١٧

دائرة مدينة الطب
الادارة العامة
الصادرة

الى / جامعة بغداد /كلية التمريض

م/تسهيل مهمة

تحية طيبة ..

اشارة الى كتابكم المرقم ١٥٨١ في٢٠١٧/٦/٨ نود اعلامكم بانه لامانع لدى دائرتنا (المركز العراقي لامراض القلب) من تسهيل مهمة التدريسيين المدرجة أسمائهم ادناة لإجراء بحثهم

للتفضل بالاطلاع ..مع التقدير

الاسماء...
١-م.د صادق عبد الحسين حسن
٢-م.د سيروان جعفر باقي

الدكتور
حسن محمد عباس
المدير العام/وكالة

نسخة منه الى/
...ير العام /شعبة التدريب والتطوير .... مع الأوليات
...كز العراقي لامراض القلب ..للعلم مع التقدير
الوصل ..١٣١٤٢١

جمهورية العراق
وزارة الصحة والبيئة
دائرة صحة بغداد / الرصافة
المدير العام
شعبة التدريب والتطوير/وحدة البحوث
العدد
التاريخ : /٧/ ٢٠١٧

محافظة بغداد
Baghdad Governorate

إلى/ م.ابن النفيس
م/ تسهيل مهمة

تحية طيبة :-
كتاب وزارة التعليم العالي والبحث العلمي جامعة بغداد / كلية التمريض المرقم ١٥٨١ في ٢٠١٧/٦/٨، يرجى تسهيل مهمة التدريسيين في كلية التمريض والمدرجة أسمائهم أدناه لغرض إجراء بحثهم الموسوم : **(العوامل الشخصية والسلوكية والبيئية المؤثرة على عدم التزام مرضى القلب بالأدوية القلبية في الردهات القلبية في مستشفيات بغداد: دراسة مقطعية)**، لاتخاذ ما يلزم لتسهيل مهمته وتزويده بما يلزم وحسب الضوابط وسياقات العمل وان لا تتحمل وزارة الصحة أية تبعات مالية للتفضل بالإطلاع وأجراء اللازم .

الأسماء:
١. م.د.صادق عبد الحسين حسن
٢. م.د. سيروان جعفر باقي

... مع التقدير ...

الدكتور
حسين عليوي كاظم
مدير شعبة التدريب والتطوير
٢٠١٧/٧/ ١٧

نسخة منه إلى:
- شعبة التدريب والتطوير / وحدة البحوث مع الأوليات .

E.Mail: Bb.ryssafa@Yahoo.Com / Brhealth2014@Gmail.Com

Appendix H The Arabic Version of the Socio-demographic Data and Medication Adherence Questionnaires

استبانة

عنوان البحث: العوامل الشخصية والسلوكية والبيئية المؤثرة على عدم التزام مرضى القلب بالادوية القلبية في الردهات القلبية في مستشفيات بغداد: دراسة مقطعية.

في بعض الاحيان يكون من الصعب على الاشخاص اخذ الادوية كما توصف من قبل الطبيب. في الاسئلة ادناه قائمة بأكثر الحالات تأثيرا. نريد ان نعرف رأيك بما يخص الممارسات اليومية لاخذك للادوية الخاصة بالامراض القلبية تحت مختلف الظروف.

رجاءأ اجب بوضع علامة (√) في المربع الاكثر قربا لرأيك الصحيح.

الفقرات	نعم	كلا
1.هل نسيت ان تأخذ ادويتك الخاصة بالامراض القلبية في اي وقت مضى؟		
2.هل اهملت تناول ادويتك الخاصة بالامراض القلبية في اي وقت؟		
3.هل توقفت عن اخذ ادويتك الخاصة بالامراض القلبية في بعض الاحيان عندما تشعر بالتحسن؟		
4.في بعض الاحيان عندما تشعر بالسوء لاخذك ادويتك الخاصة بالامراض القلبية, هل تتوقف عن اخذها؟		

رجاءأ ضع علامة (√) في المربع الذي يمثل رأيك الصحيح.

	ابدا	بعض الاحيان	اغلب الاحيان	دائما
5. كم عدد المرات التي نسيت بها اخذك لادويتك الخاصة بالامراض القلبية ؟				
6. كم عدد المرات التي قررت فيها عدم اخذك لادويتك الخاصة بالامراض القلبية ؟				
7. كم عدد المرات التي فيها توقفت فيها عن تجديد لادويتك الخاصة بالامراض القلبية ؟				
8. كم عدد المرات التي نفذ فيه لادويتك الخاصة بالامراض القلبية ؟				
9. كم عدد مرات تركك لادويتك الخاصة بالامراض القلبية قبل ذهابك للطبيب؟				
10. كم عدد المرات التي تترك فيه ادويتك الخاصة بالامراض القلبية عندما تشعر بالتحسن؟				
11. كم عدد المرات التي تترك فيه ادويتك الخاصة بالامراض القلبية عندما تشعر بالمرض؟				
12. كم عدد المرات التي تترك فيه اخذ ادويتك الخاصة بالامراض القلبية لانك مهمل؟				
13. كم عدد المرات التي غيرت فيها جرعة ادويتك الخاصة بالامراض القلبية ليلائم حاجاتك (مثال اخذ عدد حبوب اقل او اكثر من المعتادة)؟				
14. كم عدد المرات التي نسيت فيها اخذ ادويتك الخاصة بالامراض القلبية الذي من المفترض ان تأخذه اكثر من مرة واحدة باليوم؟				
15. كم عدد مرات عدم تجديدك ادويتك الخاصة بالامراض القلبية لانه يكلف الكثير من المال				
16. كم عدد المرات التي تخطط مسبقا فيها لتجديد ادويتك الخاصة بالامراض القلبية قبل ان تنفذ؟				

ليس هنالك جواب صحيح او خاطئ. لكل من الحالات المدونة في ادناه, رجاءا ما هو مدى تأكدك على اخذ ادويتك الخاصة بالامراض القلبية في كل الاوقات.

ما هو مدى قدرتك على اخذ ادويتك الخاصة بالامراض القلبية:	**لست متأكد على الاطلاق**	**متأكد قليلا**	**متأكد**	**متأكد جدا**
17. عندما تكون مشغولا في البيت				
18. عندما لا يكون هناك اي احد لتذكيرك				
19. عندما تشعر بالقلق من اخذك ادويتك الخاصة بالامراض القلبية طيلة حياتك				
20. عندما لا تكون هناك اي اعراض				
21. عندما تكون مع عائلتك				
22. عندما تذهب الى مكان عام				
23. عندما يكون اخذك لادويتك الخاصة بالامراض القلبية بين الوجبات الغذائية				
24. عند السفر				
25. عندما تأخذ ادويتك الخاصة بالامراض القلبية اكثرمن مرة واحدة باليوم				
26. عندما يكون هناك ادوية اخرى غير متعلقة بالامراض القلبية				
27. عندما تشعر بالتحسن				
28. اذا تجعلك الادوية الخاصة بالامراض القلبية تشعر بالحاجة للتبول عندما تكون بعيدا عن البيت				
رجاءا قدر مدى تأكدك وقدرتك على عمل الواجب التالي:				
29. اخذ ادويتك الخاصة بالامراض القلبية كجزأ من روتينك اليومي				

ليس هنالك اجوبة صحيحة او خاطئة. لكل من الاقوال المدونة ادناه, رجاءا قدر موافقتك او عدم موافقتك:

	موافق جدا	موافق	ليس متأكدا	غير موافق	غير موافق جدا
30. صحتي الان معتمدة على اخذ الادوية					
31. ادويتي تحميني من ان اكون اسوأ					
32. ادويتي ازعجت (عرقلت) حياتي					
33. انا في بعض الاحيان اشعر بالقلق تجاه الاثر ذو الامد الطويل للادوية					
34. الاطباء يوصفون لي الكثير من الادوية					
35. يجب على الناس ان يتوقفوا عن اخذ ادويتهم لبعض الوقت حاليا وفي المستقبل					
36. اكثر الادوية تجعل المريض مدمنا					
37. الادوية مضارها اكثر من نفعها					

المقطع الاخير من الاسئلة, رجاءا اشر الى عدد المرات التي ساعدك فيها الاشخاص الاخرين للاشهر الثلاثة الماضية.

ما هي عدد المرات التي ساعدك فيها احد ما للاشهر الثلاثة الماضية؟

	ابدا	نادرا	بعض الاحيان	معظم الاحيان	دائما
38. ساعدك في تقييم اعراضك المرضية و الاعراض الجاتبية للادويتك الخاصة بالامراض القلبية ؟					
39. قام بتذكيرك لاخذ ادويتك الخاصة بالامراض القلبية ؟					
40. قام بجلب ادويتك الخاصة بالامراض القلبية الموصوف لك ؟					
41. ساعدك لتفهم معلومات حول ادويتك الخاصة بالامراض القلبية؟					
42. تحقق معك حول ادويتك الخاصة بالامراض القلبية ؟					
43. شجعك لتتكلم مع طبيبك حول ادويتك الخاصة بالامراض القلبية اذا كان عندك اسئلة او مشاكل؟					
44. ساعدك لتصدق انه بامكانك اخذ ادويتك الخاصة بالامراض القلبية كما هو موصوف؟					
45. اتصل بك خصيصا ليسألك حول مدى تقبلك لادويتك الخاصة بالامراض القلبية ؟					

استبانة جمع المعلومات الشخصية

رجاءا, هل من الممكن تزويدنا بمعلومات اضافية عنك وعن الادوية المعتاد على اخذها.

رجاءا ضع علامة (√) امام اختيارك الاقرب الى اجابتك

العمر: .... سنة **الجنس:** ذكر ☐ انثى ☐

الحالة الوظيفية:

موظف ☐ غير موظف ☐ متقاعد ☐

السكن:

لوحدك ☐ مع الزوج/ الزوجة ☐ مع الاخرين ☐

الحالة الاجتماعية:

متزوج/ متزوجة ☐ ارمل/مطلقة ☐

اعزب ☐ منفصل/منفصلة ☐

المستوى التعليمي:

ابتدائية ☐ متوسطة ☐ اعدادية ☐

كلية/ معهد ☐ دراسات عليا ☐

الحالات المرضية الاخرى:

مرض السكري ☐ امراض مزمنة اخرى ☐

اخيرا, رجاءا اعطي بعض التفاصيل عن الادوية التي تأخذها.

الادوية الخاصة بالامراض القلبية:

علاج رقم (1)____

الجرعة اليومية____

عدد الحبوب المأخوذة:__________ عدد المرات باليوم____________________

علاج رقم (2)____

الجرعة اليومية____

عدد الحبوب المأخوذة:__________ عدد المرات باليوم____________________

علاج رقم (3)____

الجرعة اليومية____

عدد الحبوب المأخوذة:__________ عدد المرات باليوم____________________

علاج رقم (4)____

الجرعة اليومية____

عدد الحبوب المأخوذة:__________ عدد المرات باليوم____________________

علاج رقم (5)____

الجرعة اليومية____

عدد الحبوب المأخوذة:__________ عدد المرات باليوم____________________

شكرا جزيلا لاكمال الاجابة على كل الاسئلة مع امنياتنا لكم بالشفاء العاجل

Appendix I Open-ended Questions and Prompts at Six Months Post Intervention

- How did you feel about participating in motivational interviewing?

  (Prompts: Were you comfortable about talking about taking your medicines? Did it help motivate you to take your medicines as prescribed? Did it help make you more organised? feel comfortable share personal information? researcher allow you to talk freely and feel empathy toward you?).

- How was your experience receiving text messages reminders to take your heart medications?

  (Prompts: Did it encourage you to take your heart medicine in time as prescribed? Was it easy to read the text message reminders and reply to them? Was it annoying to you to receive text message reminders every week?)

- Is there anything else you'd like to tell me about taking your heart medicines as prescribed?

Appendix J Semi-Structured Interview Guide

Interview Questions:

- What medications or medicines are you currently on?

  (Prompts: If you can't remember the name, can you remember what they are for? OR – why do you take each of these? Can you tell me what they are for? If not can I remind you of them by reviewing your discharge letter?)

- Have you taken your medicines today?

  (Prompts: What time do you usually take each of your medications/ tablets/ pills?)

- How do you feel about your prescribed heart medicines?

  (Prompts: Do you feel better when you take your medications? For example, do the medicines affect your chest pain, or breathing difficulties? OR – Do you think taking medications makes you feel worse? If so, why is that?).

- How do you find taking your prescribed heart medicines? Why do you think you feel like that?

  (Prompts: What makes you decide to take your medications? OR What happens when you take- or don't take or don't take - your medicines? Does anything change? If so, what causes you to stop take your medications? (For example, side effects, not having symptoms, traveling).

- Do you find any difficulties with taking your medicines in the way they are prescribed for you? Can you tell me about this?

  (Prompts: number of medications, physical disability, forgetfulness, time constraints).

- Do you have any strategies to help you take your medications in the way they are prescribed for you?

(Prompts: Do you book a visit with your GP or cardiac specialist to discuss your medication? Do you talk with other patients about cardiac medications? Do staff explain to you how you can use your medications?).

- Is there anything that you think might make it easier for you to take your medicines the way they were prescribed for you? If yes –what are these?

  (Prompts: Any specific methods you use to remind you to take your medicine? Your family member, friends, hospital staff? Your physician, pharmacist, nurse?).

- Please describe your experience refilling your medications. How easy is it for you to get your medications refilled? If not, can you tell me why not?

  (Prompts: Do you have anybody to remind you to go and refill your medicines? Do you have someone who helps you to remember to take your tablets? If yes: Do you rely on them completely to remind you to take your tablets or is it mostly your job to remember and take your tablets?).

Appendix K Motivational Interviewing (MINT) Guide

Time:…………………………………………….
Date:…………………………………

Location:……………………………………... **Name Symbol:** ………………….

Introduction:

Thank you for agreeing to participate in this motivational interview.

You are invited to participate in this trial phase because you have already take part in phase one survey and phase two (interview). All patients who complete the survey and the interview and have a results of low level of adherence and a factors affected their medication adherence will be eligible to participate in this motivational interview.

We are asking for your help in a study that look at how cardiac patients manage with their cardiac medications. We are undertaking this study because reports show that a lot of people don't take their medicines in the way they were prescribed for them on average only 50% of medicines that are prescribed are taken as prescribed and this is a risk for people health. We want to see if we can help you with taking their medications as they have been prescribed.

The interview:

● This should take no more than 40 minutes of your time.

● I would like to ask you some questions about your personal experiences with taking medicines as a heart patient in cardiac rehabilitation.

● I would like to discuss with you some questions about your experiences with taking your medicines.

● I would like to tape record this interview, and then type up what we talk about into a computer. This will be just so I don't miss anything. Your name or any other identifying information will be removed. We will destroy the audiotape once our conversation has been typed up. Anything you say will be combined with other people's interviews and summarized. Your actual words may be used, but you will not be identifiable. Is this agreeable to you?

Interview Questions:

Interaction without motivational interviewing

- **Good morning/ afternoon. How are you doing today?**
- **We have a few things we need to go over before you finish your cardiac rehabilitation session. I'd would like to start with reviewing some of your medications and then we can talk about your experiences of taking them that can help you to prevent another heart attack.**
- **My job is to make sure you understand how and when you need to take your medications.**
- **From the list here, now we need to talk a little about how you manage to take your medicine as prescribed, do you take them regularly?**
- **You need a little time thinking about how you can manage to take all your medicines and strategies that remind you to take them without missing any. I would start with and tell you a simple way for reminding you to take your medicines such as using watch or mobile alarm or family members or friends that can help reminding you to take them. If you have any other ways to remind you that will be great.**
- **It is important to take care of your heart. You don't want to end up here in the hospital again.**

Motivational interviewing interaction

- **Did you have any concerns or anything you would like to talk about before looking at results of your answers in the survey? If yes, tell me about it?**
- **What I would like to do is talk with you about work or doesn't work for you. I am here to support you in your efforts to overcome your non-adherence problem and anything prevent you from taking your medicines as prescribed.**
- **There is a benefit of taking your medicines as schedules for you and it will save your life.**
- **We have your survey results here and I wondering if you would like to review that with me.**

- **Would you like me to explain them for you?**
- **You have a low level of medication adherence and there is some factors affecting your adherence, what your thoughts about that?**
- **You believe that all long-term medicines that are prescribed for you have side effects and disturbed your life, and you cannot tolerate it anymore.**
- **You believe that all medicines that are prescribed for you will not benefit your health and will harm you, if you stop take them, does your health improved?**
- **On one hand, you know what you need to do differently to improve your health by taking your medicines in times as scheduled for you to decrease your heart disease risks. On the other hand, your you are overwhelming by many other things in your life and are working on taking medicines as prescribed a little at a time because you want to improve your health.**
- **You should be proud of all effort you have put into taking your medicines as prescribed to you and the changes you have made in medication adherence. Small steps are what bring us to rewards in the end.**
- **I am confident that as you continue to set small goals for yourself, you will accomplish them and find a good strategy for taking your medicines as prescribed that works for you.**

Thank you for your time. It is greatly appreciated.

Appendix L The Publications of this Thesis

JAN
Informing Practice and Policy Worldwide through Research and Scholarship

REVIEW PAPER

Cardiovascular medication adherence among patients with cardiac disease: a systematic review

Ali Hussein Al-Ganmi, Lin Perry, Leila Gholizadeh & Abdulellah Modhi Alotaibi

Accepted for publication 2 June 2016

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Lecturer
Shqra University, Faculty of Applied Health Sciences, Saudi Arabia

AL-GANMI A.H., PERRY L., GHOLIZADEH L. & ALOTAIBI A.M. (2016) Cardiovascular medication adherence among patients with cardiac disease: a systematic review. *Journal of Advanced Nursing* 72(12), 3001–3014. doi: 10.1111/jan.13062

Abstract

Aims. The aim of this study was to critically appraise and synthesize the best available evidence on the effectiveness of interventions suitable for delivery by nurses, designed to enhance cardiac patients' adherence to their prescribed medications.

Background. Cardiac medications have statistically significant health benefits for patients with heart disease, but patients' adherence to prescribed medications remains suboptimal.

Design. A systematic quantitative review of intervention effects.

Data Sources. We conducted systematic searches for English-language, peer-reviewed randomized controlled trial publications via Medline, EMBASE, CINAHL, the Cochrane Library, ProQuest, Web of Science and Google Scholar published between January 2004–December 2014.

Review methods. According to pre-determined inclusion and exclusion criteria, eligible studies were identified and data extracted using a predefined form. Of 1962 identified papers; 14 studies met the study inclusion criteria, were assessed for risk of bias using the Cochrane Collaboration tool; and included in the review.

Results. Study findings were presented descriptively; due to the heterogeneity of studies meta-analysis was not possible. Included papers described interventions categorized as: (1) multifaceted; and (2) behavioural and educational, comprising: (a) text message and mail message; (b) telephone calls; (c) motivational interviewing and (d) nurse-led counselling and education.

Conclusions. Substantial heterogeneity limited the robustness of conclusions, but this review indicated that motivational interviewing, education and phone or text messaging appeared promising as means to enhance cardiac medication adherence. Future research should integrate multifaceted interventions that target individual behaviour change to enhance adherence to cardiovascular medications, to build on the beneficial outcomes indicated by this review.

Keywords: adherence, cardiac disease, cardiovascular medication, education, motivational interviewing, nurse-led intervention, nursing, systematic review, text message

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Behaviour change interventions to improve medication adherence in patients with cardiac disease: Protocol for a mixed methods study including a pilot randomised controlled trial

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A B S T R A C T

Background: Suboptimal adherence to medication increases mortality and morbidity; individually tailored supportive interventions can improve patients' adherence to their medication regimens.
Aims: The study aims to use a pilot randomised controlled trial (RCT) to test the hypothesis that a theory-based, nurse-led, multi-faceted intervention comprising motivational interviewing techniques and text message reminders in addition to standard care will better promote medication adherence in cardiac patients compared to standard care alone. The pilot study will assess self-reported adherence or non-adherence to cardiovascular medication in patients referred to a cardiac rehabilitation program following hospital admission for an acute cardiac event and test the feasibility of the intervention. The study will examine the role of individual, behavioural and environmental factors in predicting medication non-adherence in patients with CVD.
Methods: This is a mixed- methods study including a nested pilot RCT. Twenty-eight cardiac patients will be recruited; an estimated sample of nine patients in each group will be required for the pilot RCT with 80% power to detect a moderate effect size at 5% significance, and assuming 50% loss to follow-up over the six month intervention. Participants will complete a paper-based survey (Phase one), followed by a brief semi-structured interview (Phase two) to identify their level of adherence to medication and determine factors predictive of non-adherence. Participants identified as 'non-adherent' will be eligible for the pilot randomised trial, where they will be randomly allocated to receive either the motivational interview plus text message reminders and standard care, or standard care alone.
Discussion: Nurse-led multi-faceted interventions have the potential to enhance adherence to cardiac medications. The results of this study may have relevance for cardiac patients in other settings, and for long-term medication users with other chronic diseases.

1. Introduction

World-wide, the prevalence of cardiovascular disease (CVD) is increasing rapidly because of changes in population lifestyles (Hauptman, 2008), resulting in major concerns for community health (Zhu, Wang, Zhu, Zhou, & Wang, 2015). Cardiovascular disease has emerged as a leading cause of death and disability in Australia (Nichols, Peterson, Alston, & Allender, 2014), affecting one in six people and responsible for 16% of the nations' total disease burden. It is the main reason for rehospitalisation (Australian Institute of Health and Welfare, 2014); costs in 2004–5 of AU$5.94 billion accounted for 11% of Australia's total health expenditure (Australian Institute of Health and Welfare, 2010). Quality of life has been shown 7to improve for patients with CVD referred to a comprehensive cardiac rehabilitation and secondary prevention program (Shepherd & While, 2012). These programs comprise recovery and preventative activities aimed at modifying cardiac risk factors and enhancing physico-psycho-social function to reduce the risk of subsequent cardiac events (Woodruffe et al., 2014). Cardiac rehabilitation enables changes in patient lifestyles

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Medication adherence and predictive factors in patients with cardiovascular disease: A comparison study between Australia and Iraq

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ABSTRACT

Background: Adherence to cardiac medication regimes is essential for effective treatment of cardiovascular disease but is unsatisfactory in Australia and little studied in Iraq.

Aim: This study evaluated and compared adherence to cardiac medications and potentially predictive factors based on the Theory of Planned Behaviour (TPB) in patients with cardiovascular disease admitted to hospital and attending cardiac services in Australia and Iraq.

Methods: A cross-sectional multi-centre comparative study involving 246 cardiac patients was conducted in Australia (one hospital in Sydney) and Iraq (three cardiac hospitals in Baghdad) between October 2016 and December 2017. Adherence to medications and related factors were examined using established, validated questionnaires, formally translated and validated into Arabic for Iraqi participants. Binary logistic regression was conducted to determine those factors independently predictive of cardiac medication adherence, in Australia and Iraq.

Findings: A significantly higher proportion (64.3%) of Iraqi than Australian (37.5%) cardiac patients reported medium/low levels of adherence to their cardiac medications. After adjusting for confounding factors, the ability to correctly self-administer and refill medications, and beliefs about cardio-protective medication were identified as independent predictors of cardiac medication adherence behaviour in both Australian and Iraqi participants. In Iraq, patients recruited from out-patient cardiac clinics were significantly more likely to report adherent behaviours that patients recruited as in-patients of the cardiac ward.

Conclusion: Non-adherence to cardiac medications differed but was sub-optimal in both Australian and Iraqi patient samples, in both countries, adherence was associated with patients' beliefs about medications, and ability to self-administer and refill medications. Clinical nurses and pharmacists need to investigate these factors at every point in the cardiac trajectory to optimise medication adherence.

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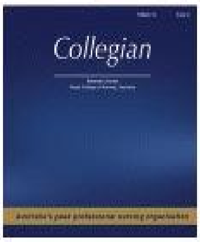

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